An Epidemiological Investigation into the Onset, Course and Outcome of Psychotic Major Depression and Schizoaffective Disorder, Depressed Type

Heslin, Margaret

Awarding institution:
King's College London

For Anne Lucy Murphy

An Epidemiological Investigation into the Onset, Course and Outcome of Psychotic Major Depression and Schizoaffective Disorder, Depressed Type

Margaret Heslin

Submitted for the award of PhD in Epidemiology

Institute of Psychiatry, Kings College London,
University of London

October 2013

Abstract

There is very little research on the psychosocial risk factors associated with psychotic major depression (PMD) and schizoaffective disorder, depressed type (SAD). Although there is much more research on the course and outcomes of these disorders, the studies have significant methodological limitations. Therefore, this thesis aimed to investigate the following while improving on the limitations of previous research: 1) the risk factors associated with PMD and SAD with a focus on psychosocial risk factors; and 2) the long-term course of illness and outcomes in cases with PMD and SAD.

A case control study of incident psychosis cases was used to examine psychosocial risk factors in PMD and SAD cases compared with schizophrenia and bipolar disorder cases. A cohort study following up all cases identified in the case control study was conducted to investigate course of illness and outcomes.

Findings on the risk factors suggest that less psychosocial risk factors are involved in the aetiology of PMD and SAD compared with schizophrenia and bipolar disorder. Exploratory analyses of life events indicate that humiliation life events could be an important factor in the development of PMD and requires further research. Findings on outcomes suggest that PMD cases are more likely to self-harm and attempt suicide but are less likely to use inpatient services and have a lower proportion of compulsory admissions. These findings have important clinical implications. Findings on risk factors and outcomes in SAD cases are similar but a lack of power due to low numbers limits the interpretation of the findings.

Important differences in both the risk factors and outcomes analyses were identified when based on the baseline and lifetime diagnoses. This highlights the importance of accounting for diagnostic change when examining these diagnostic groups.

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Acknowledgements

There are many people who contributed to this thesis and supported me in this venture. First and foremost, for providing unwavering support and love, I would like to thank K.C.

I have been very fortunate to have a group of incredibly supportive friends and colleagues who have provided their support and occasional honest opinion: Laura Cole; Georgia Black; Laura Nellums; Victoria Bird; Kylee Trevillion; Manuela Jarrett; Barbara Barrett; Helen Gilburt; Jason Tsang; and Grant McQueen.

I would like to thank my mentor, Helen Fisher, for her invaluable advice and support, and Anita Patel and Sarah Byford who provided huge amounts of support.

Statistical advice was most welcome and kindly provided by Ulrich Reininghaus, Leonardo Koeser and Michael Dewey.

I am grateful to my supervisors, Dr Craig Morgan and Professor Tom Craig for their guidance and support over the last four years. I am also grateful to all the many researchers who worked on the AESOP study on which this thesis is based, but especially to the students who worked as committed research assistants: Adanna Onyejiaka; Chidi Onyejiaka; Roopal Desai; and Suzan Hassan. Finally, this thesis would not be possible without the individuals who participated in the AESOP study.

Abbreviations

AESOP – Aetiology and Ethnicity in Schizophrenia and Other Psychoses study

PMD – Psychotic major depression

SAD - Schizoaffective disorder, depressed type

SAM - Schizoaffective disorder, manic type

SA – Schizoaffective disorder

SZ - Schizophrenia

SZFORM - Schizophreniform

BP – Bipolar disorder

NPMD – Non-psychotic major depression

CHAPTER 1. Introduction

"Psychotic depression is a common and costly condition, but with no accepted best practice guidance for its management. More attention needs to be focused on this largely under-researched group."[1]

Crebbin et al. (2008)

1.1. Aims of the thesis

Crebbin et al. claim that cases with a diagnosis of psychotic major depression are a "...largely under-researched group".[1] Therefore, the purpose of this thesis was to explore two key areas of research in this group: aetiology (with a particular focus on psychosocial risk factors); and long-term outcomes.

1.2. Outline of thesis

Chapter 2 of this thesis discusses the diagnosis of psychotic major depression (PMD) and the overlap with a similar diagnosis: schizoaffective disorder, depressed type (SAD). This highlights reasons for the decision to examine both diagnoses within this thesis. This chapter goes on to discuss the gaps in the literature which form the basis for this thesis. There is also some discussion about the key methodological issue of diagnostic stability.

Chapters 3 and 4 are reviews of the literature. Chapter 3 discusses the concept of social adversity. This chapter goes on to review the literature on social adversity in the aetiology of depression and psychosis, and where available in PMD and SAD diagnostic groups specifically. Chapter 4 is a systematic review of the literature on outcomes in PMD and SAD cases. Following a review of the literature, a section discussing the methodological limitations of previous research highlights how the study reported in this thesis sought to improve on previous research.

Chapter 5 describes the methodology used within this thesis. The methods are split into three parts: an overview of the AESOP study; a section on the case-control section of the thesis; and a section on the cohort section of this thesis. The overview describes the

context of the AESOP study, the data from which is the basis of this thesis. The case-control section describes the methods which were used to test hypotheses on psychosocial risk factors in PMD and SAD cases. The cohort section describes the methods used to test hypotheses on long-term course and outcomes in PMD and SAD cases.

Chapters 7 and 8 are results chapters. Chapter 7 presents results from the case-control study which aimed to test hypotheses around psychosocial risk factors. This is first based on baseline diagnoses and then based on the lifetime diagnoses, with a section comparing the two. Chapter 8 describes the results from the cohort study which aimed to test hypotheses about long-term outcomes of PMD and SAD cases compared with schizophrenia and bipolar cases. Similar to chapter 7, the results are first based on baseline diagnoses and then based on lifetime diagnoses.

Finally, chapter 8 summarises the salient results and then explores the methodological considerations, comparisons to previous literature, theoretical implications and clinical implications. This is done separately for the case-control and cohort sections of the thesis. Future research and final conclusions are then considered.

1.3. Statement of the candidate's contribution

The ÆSOP study was originally created by Professor Robin M Murray and Professor Julian Leff (Institute of Psychiatry, KCL). When I began on the ÆSOP study I examined data that had been collected at baseline and data that was being collected at follow-up. I then examined the literature on psychosis and found that there was a gap in the research on PMD. This information was then drawn together to create an outline of a PhD to investigate what has been described here. This was all done under the guidance

of Dr. Craig Morgan and Professor Tom Craig. Specifically, I developed the study hypotheses and decided to investigate differences in findings when based on baseline and lifetime diagnoses, which, as discussed throughout the thesis, is an important methodological advance.

I was fully involved in all aspects of the cohort phase of the study, including tracing, consenting and collecting data from participants for over 2 years. I personally traced and recruited cases from all over the UK and even traced, recruited and conducted telephone interviews with one case in New Zealand and another in Norway.

I have made a substantial contribution to the completion of Life Chart assessments with over a third of the London Life Charts completed by myself (n124). With an average follow-up of 10 years, this involved reading and summarising over 1,240 years of clinical notes. I have also been involved in diagnostic and life chart consensus meetings for over 200 participants.

I entered all of the data from the cohort phase of the study into Access databases and conducted all data cleaning. I conducted all the data analysis presented in this thesis under the guidance of Dr. Craig Morgan and Professor Tom Craig.

CHAPTER 2. Background

"What yesterday appeared to be generally accepted and established, was today, to some, at best, a precarious working-hypothesis, to others a dogma to be fought, and to others again, a fairy tale from the remote past."[2]

Neki (1963)

2.1. Myths in the literature...

Two recent works dedicated to the understanding of PMD begin their opening chapter by recounting the story of Andrea Yates.[3, 4] Andrea was a woman who drowned her five children in the bathtub one day as a result of her experiencing PMD. According to the author of the first book, *"psychotic depression is highly dangerous"* as patients contemplate suicide, and *"psychotic depressions can also be risky for others… periodically there are terrible stories of psychotically depressed parents who murder their children…".*[4] A much earlier journal article states: *"Another reason for admitting severely depressed patients to hospital is that on occasion they murder their relatives or friends in an attempt to spare them imagined pain".* [5]

These authors paint a bleak prognostic picture for patients and their families who receive a diagnosis of PMD. A vital question is whether the prognostic picture for patients with a diagnosis of psychotic depression is as grim as these books would have us believe. Furthermore, what is the relationship between the prognosis of PMD and it's very close cousin, SAD. The purpose of this thesis was to examine the long-term outcomes for these overlapping disorders and to examine who is at risk of receiving these diagnoses.

Henceforth, psychotic major depression will be referred to as PMD and schizoaffective disorder, depressed type will be referred to as SAD.

2.2. Diagnosis of PMD and SAD

Diagnoses have been evolving since the start of psychiatry and are still evolving today.[2] PMD and SAD are no exception to this.[6] A comprehensive history of PMD is given by

Swartz and Shorter[4] and the historical context of schizoaffective disorder has already been documented by Tsuang and Simpson,[7] and Procci.[8] Therefore, only the current most widely used diagnostic classification systems in Europe and the US will be examined: the International Classification of Diseases (ICD); and Diagnostic and Statistical Manual of Mental Disorders (DSM).

2.2.1. ICD development

The International Classification of Diseases (ICD) manual by the World Health Organisation (WHO) is a classification system which has undergone radical changes over its history. Before 1977 the WHO in its ICD manual simply listed diagnoses under certain headings.[9-11] There were no criteria or descriptions of what was meant by each diagnosis, therefore leading to possible confusion and unreliable diagnoses among those using these tools, which would include clinicians and researchers. Under its depressive section (301.1), ICD-6[9] (published in 1948) listed 'insanity or psychosis, manic-depressive, depressive'. Schizo-affective psychosis (300.6) was listed as a subtype of schizophrenic disorders (dementia praecox) and specified the subtypes of mixed schizophrenic and manic-depressive psychosis, schizo-affective psychosis and schizothymia. ICD-7[10] (published in 1957) was the same as ICD-6 in terms of mention of depression and schizo-affective psychosis. ICD-8[11] (published in 1967) heralded the first mention of the term 'psychotic depression' in the ICDs which is included as a subcategory of manic-depressive psychosis, depressed type (296.2). Schizo-affective type (295.7) was still listed as a subtype of schizophrenia. It had the subtypes of mixed schizophrenic and affective psychosis and schizo-affective psychosis but schizothymia which was in earlier editions had been removed.

ICD-9,[12] (published in 1977) by contrast, included a short description of what was meant by each item. However, without detailed information, the items were still open to interpretation, leading to the possibility of heterogeneous groups being labelled with the same diagnosis. ICD-9[12] included 'manic-depressive psychosis, depressed type' (296.1) with a description of the disorder and 'depressive psychosis' and 'psychotic depression' as subgroups, although these terms had no definition. Schizoaffective disorder (295.7) was highlighted as a subtype of schizophrenic psychoses. It included the subtypes cyclic schizophrenia, mixed schizophrenic and affective psychosis, schizo-affective psychosis and schizophreniform psychosis, affective type. There were no specific diagnostic criteria for the subtypes, however there was a description of schizoaffective type: *"A psychosis in which pronounced manic or depressive features are intermingled with schizophrenic features and which tend towards remission without permanent defect, but which is prone to recur. The diagnosis should be made only when both the affective and schizophrenic symptoms are pronounced"*.[12]

Despite the inclusion of the terms depression and psychosis in ICD-6, -7, -8 and -9, these descriptions would not be recognised as PMD in modern terms; *psychosis* was used only to refer to severe impairment in functioning or to distinguish from *neurotic* disorders.[13] ICD-10[14] (published in 1993) was the first edition to explicitly explain what was meant by each diagnosis by giving a list of symptoms which were used as criteria. This was the first overt description of what is currently understood by the term 'psychotic depression' to come from the ICD diagnostic literature. This was an important development as it meant it was then possible for clinicians and researchers to discuss PMD and know that they were referring to the same cluster of symptoms and the same clinical picture.

ICD-10 has two versions: *Clinical descriptions and diagnostic guidelines*;[15] and *Diagnostic criteria for research*.[14] They are exactly what the titles suggest: *clinical descriptions and diagnostic guidelines* is a descriptive account of what is meant by each diagnostic name; and the *Diagnostic criteria for research* gives exact criteria that a patient must fulfil to receive each diagnosis.

ICD-10[14] includes PMD under the depression section. An episode of PMD is included as a severe depressive episode with psychotic symptoms (F32.3).[14] This must include at least two of the following: depressed mood; loss of interest and enjoyment; or increased fatigability. These must be accompanied by the following:

a) at least 4 of the following:
    I. reduced concentration and attention;
    II. reduced self-esteem and confidence;
    III. ideas of guilt and unworthiness;
    IV. bleak and pessimistic views of the future;
    V. ideas or acts of self-harm or suicide;
    VI. disturbed sleep;
    VII. diminished appetite.
b) Lasting at least 2 weeks unless very severe or very rapid onset.
c) Interference with daily activities, i.e., work, social, domestic life.
d) Plus delusions, hallucinations or depressive stupor.

Delusions and hallucinations may be specified as mood-congruent or mood-incongruent. ICD-10[14] specifies that delusions usually surround ideas of poverty, sin or imminent disaster for which the patient is responsible. Auditory hallucinations are usually defamatory or accusatory, and olfactory hallucinations can be of rotting filth or

decomposing flesh. Depressive stupor must be differentiated from catatonic schizophrenia, dissociative stupor and organic forms of stupor.

To have a diagnosis of recurrent depressive disorder, current episode severe with psychotic symptoms the patient must have had at least two episodes of the above which lasted a minimum of two weeks and were separated by several months without mood disturbance. Patients must also have no history of mood elevation or over activity that fulfils criteria for mania, but the diagnosis is still valid if there is evidence of brief episodes of mild mood elevation and over activity which fulfil criteria for hypomania immediately after a depressive episode.

In contrast to all the other ICDs, the ICD-10[15] does not include schizoaffective disorder as a subtype of schizophrenia but as a psychotic disorder distinct from schizophrenia (F25). The *Diagnostic criteria for research* version of the ICD-10[14] states the criteria for gaining a diagnosis of schizoaffective disorder is as follows:

a) at criteria met for one of the affective disorders to a moderate or severe degree
b) symptoms from at least one of the groups below must be clearly present for a period of at least 2 weeks
    I. thought echo, insertion, withdrawal or broadcast
    II. delusions of control, influence or withdrawal
    III. hallucinatory voices giving a running commentary on the patient's behaviour or discussing the patient or other hallucinatory voices coming from some part of the body
    IV. persistent delusions of other kinds that are culturally inappropriate but not merely grandiose or persecutory
    V. grossly irrelevant or incoherent speech

VI. intermittent but frequent catatonic behaviour

c) criteria a and b must be present and prominent in the same episode of the disorder and concurrently for at least part of the episode

The ICD-10[14] goes on to split schizoaffective disorder (for the first time) into subtypes linked to affective symptomatology: schizoaffective disorder, manic type (F25.0); schizoaffective disorder, depressive type (SAD; F25.1); schizoaffective disorder, mixed type (F25.2); other schizoaffective disorders (F25.8); and schizoaffective disorder, unspecified (F25.9). To gain the diagnosis of SAD, a patient must meet the criteria for schizoaffective disorder and the criteria for a depressive disorder – moderate severity at least.

2.2.2. DSM development

Dissatisfaction among American psychiatrists with the mental disorders proposed by ICD-6[16] prompted the United States Public Health Service (USPHS) and American Psychiatric Association (APA) to create the Diagnostic and Statistical Manual of Mental Disorders (DSM). DSM-I[17] (published in 1952) and DSM-II contained descriptions of disorders only. DSM-I included two categories that correspond to today's definition of PMD: psychotic depressive reaction (defined as severe depression and gross misinterpretations of reality, including delusions and hallucinations); and involutional psychotic reaction (restricted to the involutional period, it was characterised by depression without a previous history of manic depressive episodes and could be manifested by a number of symptoms including delusional ideas). DSM-II[18] (published in 1968) included the same two diagnoses but with slight modifications: psychotic depressive reaction now included impairment of function; and involutional psychotic reaction was replaced by involutional melancholia (characterized by worry, anxiety,

agitation, insomnia and delusional guilt or somatic preoccupations). Involutional melancholia was said to be distinguishable from schizophrenia as impaired reality testing was due to a disorder of mood and from psychotic depressive reaction in that the depression was not due to some life event. Swartz and Shorter[4] claim that the psychotic reference in DSM-II to psychotic depressive reaction was actually an indicator of severity. This means that researchers and clinicians referring to this disorder would be referring to something different from what would be understood as PMD today.

In terms of schizoaffective disorder, DSM-I[17] designated schizoaffective as a subtype of schizophrenia (x27) – schizophrenic reaction, schizo-affective type, which described cases showing a significant mix of schizophrenic and affective reactions, although the picture may be predominantly schizophrenic with pronounced elation or depression, or predominantly affective with schizophrenia-like thinking or bizarre behaviour. DSM-II[18] differed only in that, schizoaffective was schizo-affective, excited (295.73) and schizophrenia, schizo-affective, depressed (295.74).

The DSM-III[19] (published in 1980) was the first classification system which had operational definitions of psychiatric disorders and Mack et al. [16] claim it was independent of aetiology and theory. The DSM-III[19] allowed for a diagnosis of major depressive episode as dysphoric mood or loss of interest or pleasure in all or almost all usual activities and pastimes, plus four of the following:

- Significant weight loss or weight gain or increased / decreased appetite;
- Insomnia or hypersomnia;
- Psychomotor agitation or retardation;
- Loss of interest or pleasure in usual activities or decrease in sexual drive;
- Fatigue or loss of energy;

- Feelings of worthlessness or excessive/inappropriate guilt;
- Diminished ability to think or concentrate, or indecisiveness;
- Recurrent thoughts of death or suicidal thoughts or attempts.

The definition in this version included a further specifier of psychotic features if there is a gross impairment of reality, i.e. delusions or hallucinations, or depressive stupor. The hallucinations and delusions can be further specified as either mood congruent psychotic features or mood incongruent psychotic features.

There was little change in subsequent DSM iterations with DSM-III-R[20] (published in 1987) only removing stupor from the criteria and DSM-IV[21] (published in 1994) stipulating severe depression. That brings us to the current version of the DSM. The DSM-IV-TR[22] includes the same criteria as previous editions, but adds information. It states that hallucinations are typically auditory, transitory, not elaborate and normally berating the person for their shortcomings. The content of delusions and hallucinations are commonly consistent with depressive themes. These mood congruent delusions include delusions of guilt, deserved punishment, poverty and nihilistic or somatic delusions. Mood incongruent delusions are less common and include things such as persecutory delusions and delusions of thought insertion, thought broadcasting and control.

In terms of schizoaffective disorder, the DSM-III[19] moved schizoaffective disorder from a subtype of schizophrenia to psychotic disorders not elsewhere classified. There were no diagnostic criteria for this diagnosis included here and it is designated to be used when *"the clinician is unable to make a differential diagnosis with any degree of certainty between Affective Disorder and with Schizophreniform Disorder or*

Schizophrenia".[19] DSM-III-R[20] was the first to specify diagnostic criteria for schizoaffective disorder (295.70). DSM-III-R emphasizes temporal relationships between the schizophrenic and affective symptoms: cases who do not meet criteria for schizophrenia or mood disorders but who have experienced schizophrenic and mood symptoms at one time point and have presented with psychotic symptoms in the absence of mood symptoms at another time point. Specific criteria were as follows:

a) a disturbance during which, at some time, there is either a Major Depressive or a Manic Syndrome concurrent with symptoms that meet the A criterion of Schizophrenia.
b) during an episode of the disturbance, there have been delusions or hallucinations for at least two weeks, but no prominent mood symptoms.
c) schizophrenia has been ruled out, i.e., the duration of all episodes of a mood syndrome has not been brief relative to the total duration of the psychotic disturbance.
d) it cannot be established that an organic factor initiated and maintained the disturbance.

There are two subtypes listed; bipolar type (previous or current manic syndrome); and depressive type (no current or previous manic syndrome).

DSM-IV[21] again emphasizes a temporal element as important, and specific diagnostic criteria are stated as follows:

a) an uninterrupted period of illness during which, at some time, there is either a Major Depressive Episode, a Manic Episode or a Mixed Episode concurrent with symptoms that meet Criterion A for Schizophrenia. (Note: The Major Depressive Episode must include Criterion A1: depressed mood).

b) during the same period of illness, there have been delusions or hallucinations for at least 2 weeks in the absence of prominent mood symptoms.
c) symptoms that meet criteria for a mood episode are present for a substantial portion of the total duration of the active and residual periods of the illness.
d) the disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Although the wording is different for these criteria they are essentially the same as for DSM-III-R.[20] Like DSM-III-R the two subtypes stated are bipolar type (applies if a manic or mixed episode is part of the presentation) and depressive type (applies if only major depressive episodes are part of the presentation in the absence of mania). Schizoaffective disorder is the same in DSM-IV-TR[22] as it is in DSM-IV.[21]

2.3. Symptom overlap between PMD and SAD

PMD overlaps with SAD in terms of symptoms and only a few criteria distinguish them from one another. Within the ICD-10[14] patients must have met criteria for a depressive disorder to a moderate or severe degree plus experience thought echo, insertion, withdrawal or broadcast; delusions; auditory hallucinations; grossly irrelevant / incoherent speech; or catatonic behaviour within the same episode concurrently for at least part of the episode to meet a diagnosis of SAD. Within DSM-IV-TR[22] to meet criteria for a diagnosis of SAD, patients have to have experienced a depressive episode (which is present for a substantial proportion of the time) concurrent with at least one of either delusions, hallucinations, disorganized speech, disorganised or catatonic behaviour and negative symptoms. The psychotic symptoms must be experienced in the absence of a mood component for at least two weeks.

The literature around PMD is confused as each study uses a different diagnostic system to determine diagnosis and each system has slightly different criteria (e.g., ICD-10,[14] DSM-IV-TR,[22] Research Diagnostic Criteria,[13] Feigner criteria[23]). Some studies even modified the criteria of a diagnostic system. This has led to some studies claiming to measure PMD but actually capturing groups with PMD and SAD cases.

In addition, symptoms of depression are evident in those with schizophrenia, often secondary to the schizophrenia. A study by Wassink et al.[24] conducted a 5- year follow up study with patients with recent-onset schizophrenia. They found that less than 12% of cases had no symptoms of depression, more than one-third of the subjects met the criteria for a major depressive episode at the time of intake and the majority of cases had four symptoms of depression to at least a moderate degree. So, diagnosing PMD and SAD is far from straightforward – an issue rarely acknowledged in the literature.

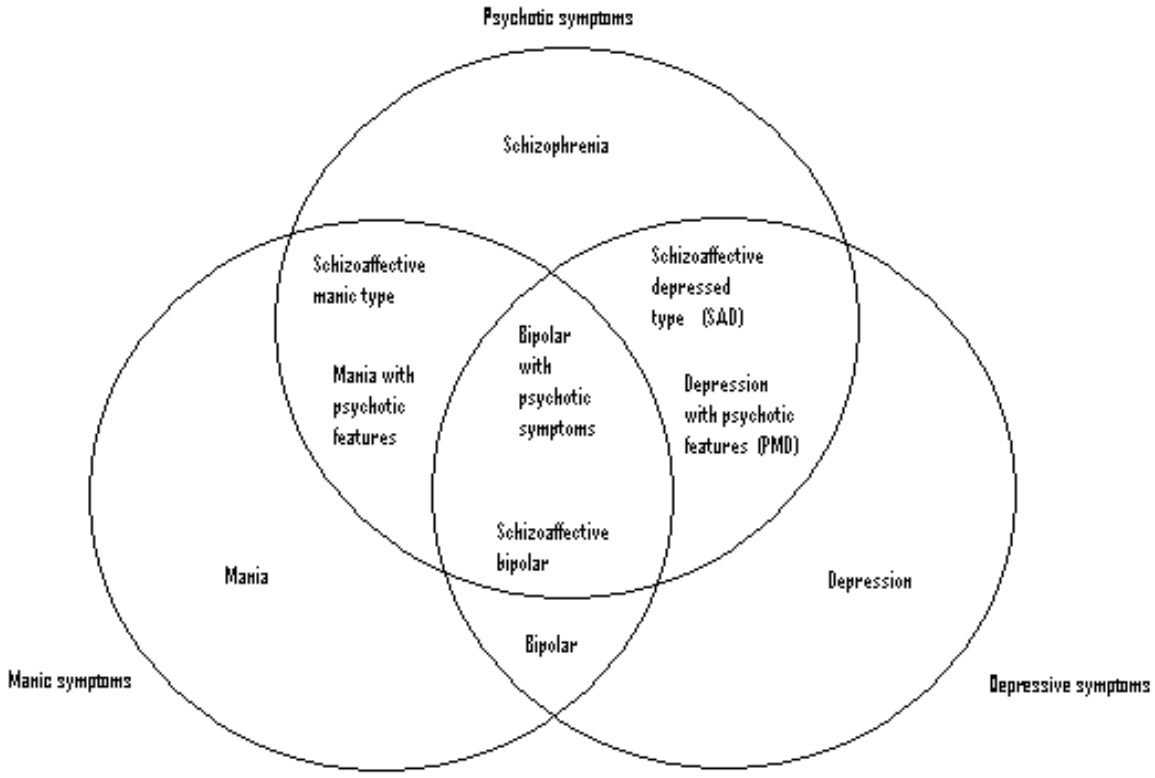


Figure 2-1: Representation of symptom overlap of psychotic and affective disorders

Figure 2-1 is a representation of symptoms overlap of affective and psychotic diagnoses. From this it can be seen that PMD and SAD inhabit the same symptomatic cluster of depressive symptoms and psychotic symptoms. However, the symptom picture is rarely so clear with depressive symptoms being common in schizophrenia and so the representation is very simplistic and compartmentalised. However, the overlap with the 2 disorders is clear and the distinction between the two seems arbitrary, giving rise to the aims of this thesis: to use both diagnoses to follow-up patients with substantial depressive and psychotic symptoms.

2.4. Prevalence and incidence

2.4.1. PMD

General population estimates of the prevalence of PMD have been examined. Ohayon and Schatzberg reported a lifetime prevalence of PMD in the general population of the United Kingdom, Germany, Italy, Portugal, and Spain between 1994 and 1999. They measured PMD using Sleep-EVAL, a software system comprised of a standard questionnaire including questions to match criteria from the DSM-IV. This was collected via telephone interview. The authors reported the lifetime prevalence of PMD in these countries to be 0.4% (95% CI = 0.35-0.54%) with slightly higher rates for the UK at 0.5% (95% CI = 0.3%–0.7%).[25] Perala et al.[26] also reported a lifetime prevalence of PMD in the general population of Finland. They conducted medical examinations which included an assessment of mental disorder using the Composite International Diagnostic Interview. These were conducted with a random sample of individuals drawn from the National Population Register (which had a 93% response rate). The authors also reported an approximate lifetime prevalence of PMD to be 0.4% (95% CI = 0.24-0.51%).[26] This is compared with 0.87% (95% CI = 0.68-1.11%) for schizophrenia,

0.32% (95% CI = 0.21-0.46%) for schizoaffective disorder (SAD not reported) and 0.12% (95% CI = 0.06-0.23%) for bipolar I disorder with psychotic features.

Proctor et al.[27] conducted an incidence study of all first episode psychosis cases referred to a single trust in the North of England between 1998 and 2001 using an observational database and ICD diagnoses. The authors reported that the 'commonest diagnosis' was PMD, accounting for 19% of all new cases. This was compared with 11% for paranoid schizophrenia and 7.5% for bipolar disorder. However, the authors do not report the incident rates for PMD. The authors also report subtypes of schizophrenia separately (e.g. paranoid schizophrenia and schizophrenia unspecified).

Baldwin et al.[28] examined incidence of psychosis in two rural counties in the Republic of Ireland from May 1995 to April 2003. DSM-IV diagnosis was achieved by consensus of the team following patient evaluation using the Structured Clinical Interview for DSM-III-R or via clinical notes when cases refused interview. Six months after presentation clinical material was reviewed to confirm or modify the initial DSM-IV diagnosis, again using consensus by the team. The authors reported an annual incidence (based on diagnosis at six months) of 6.4 per 100,000 population aged 15 or over (95% CI 4.5-8.7) for PMD cases compared with 7.0 per 100,000 population aged 15 or over (95% CI 5.1-9.4) for schizophrenia cases. However, the estimate for schizophrenia increased to 10.8 per 100,000 (95% CI 8.3-13.7) if all schizophrenia spectrum psychoses were included.

From these incidence studies, it appears that PMD occurs at a similar rate to schizophrenia. However, Kirkbride et al.[29] conducted a systematic review and meta-analysis of the incidence of all psychotic disorders in England and reported that based

on the four studies with incidence data on PMD, the pooled estimates for PMD was 5.3 (95% CI 3.7-7.6) per 100,000 person years compared with 3.7 per 100,000 person years (95% CI 3-4.5) for bipolar and 15.2 per 100,000 person years (95% CI 11.9-19.5) for schizophrenia. This review and meta-analysis suggests that PMD is less common than schizophrenia.

2.4.2. SAD

Estimates of the incidence and prevalence of SAD are rare. Most studies include schizoaffective disorder (SA) overall (a mix of schizoaffective disorder depressed type, manic type, mixed type, other and unspecified). The DSM-IV[21] states that details on the exact prevalence are unknown but SA appears to be less common than schizophrenia.

Brockington et al.[30] reviewed the case notes of 3,800 first admission patients and then interviewed approximately 600 of these cases approximately 4 days after admission. Those cases who were positive for both depression and schizophrenic or paranoid symptoms had a full psychiatric evaluation using the Present State Examination (version 9). The authors reported that 2% of the 3,800 cases admitted met criteria for schizodepressive illness.

Procter et al.[27] (mentioned above) in their incidence study of all first episode psychosis cases referred to a single trust in the North of England reported that the diagnosis of schizoaffective disorder was given to just 1.8% of all cases. This was the least common diagnosis apart from alcohol related psychoses. This was compared with 19% for PMD cases, 11% for paranoid schizophrenia, and 7% for bipolar disorder. However, the authors do not report the incident rates for schizoaffective cases.

Brockington and Leff conducted a review of case notes of all first admission patients from the Camberwell catchment area in 1973-4 and compared different diagnostic systems.[31] They reported that schizoaffective cases made up 10% of the first admission patients from the Camberwell catchment area in 1973-4. This translated into estimated upper and lower limits of incidence of schizoaffective disorder of 0.3 to 5.7 per 100,000 per year. This compared with an incidence of schizophrenia of 7.3 to 15.0 per 100,000 and of mania of 1.7 to 3.3 per 100,000. The authors concluded that the incidence of schizoaffective disorder was probably around a quarter of that of schizophrenia and comparable to that of mania.[31] The authors reported that 12 cases met criteria for schizodepressive illness form a catchment population of 150,000 over 2 years.[31]

The studies in this section indicate that not only is schizoaffective disorder relatively rare compared with other psychotic disorders, but also SAD is very rare, although comparative rates are not available.

2.5. Gaps in the literature

PMD and SAD are still relatively under-researched diagnoses. A crude search at the beginning of this PhD on Medline revealed there are just over 5000 articles involving PMD, only 45 articles mentioning SAD but almost 100,000 articles involving schizophrenia. The lack of research on PMD and SAD compared with schizophrenia can also be illustrated by National Institute for Health and Clinical Excellence (NICE) guidelines. The guideline for the treatment and management of depression in adults by NICE[32] include the following paragraph on the management of depression with psychotic symptoms:

"1.10.3.1 For people who have depression with psychotic symptoms, consider augmenting the current treatment plan with antipsychotic medication (although the optimum dose and duration of treatment are unknown)".[32]

This is the only section on the treatment of PMD.

The NICE guidelines on schizophrenia[33] state they are concerned with the treatment and management of schizophrenia and related disorders including schizoaffective disorder. Despite this claim, there is no specific guidance on the treatment of schizoaffective disorder let alone SAD. Schizoaffective disorder is often excluded from studies on schizophrenia. However, even when schizoaffective disorder is included in a study, it is included in the schizophrenia group and therefore any important differences between schizophrenia and schizoaffective disorders are not identified.

2.5.1. Risk factors

Understanding the risk factors involved in the aetiology of a disorder is vitally important. It could lead to faster or better recovery via effective interventions.[34] Knowledge about risk factors may also aid in the understanding of the mechanisms underlying a disorder which could also eventually lead to prevention.[35] This thesis aimed to focus on psychosocial risk factors as they have been found to be prominent in non-psychotic depression[36-38] and psychosis.[38-41] Chapter 3 discusses the fact that there are very few studies on psychosocial risk factors in psychosis which include PMD and SAD cases as diagnoses independent from other psychoses. The chapter will also discuss the methodological limitations surrounding these studies and the consequent need for more methodologically robust studies on the risk factors involved in PMD and SAD.

2.5.2. Course and outcome

Prognosis is a key piece of information. Prognosis allows patients and their families to know what to expect and plan their future, and provides a basis for treatment decisions.[42] Chapter 4 discusses the numerous papers that have examined course of illness and outcomes in PMD and SAD cases. There is also a discussion of the methodological limitations of these studies which make interpretation of the findings difficult and, hence, indicate the need for more methodologically robust studies on the long term outcomes of PMD and SAD.

2.6. Issues with diagnostic systems

Diagnosis in psychiatry has frequently come under fire. Robins and Guze[43] discussed how clinical features, outcome and family history have to be used to create psychiatric nosological categories in the absence of clinical tests. The National Institute of Mental Health recently criticised the validity of DSM-5 and stated "Unlike our definitions of ischemic heart disease, lymphoma, or AIDS, the DSM diagnoses are based on a consensus about clusters of clinical symptoms, not any objective laboratory measure".[44] Van Os and Tamminga[45] stated that the numerous diagnostic categories that exist were created originally to bring order and aid scientific communication. They are designed to refer to broadly defined psychopathological syndromes rather than biologically defined diseases, but over time they have undergone a process of reification and become assumed to be concrete disease entities. By classifying patients arbitrarily into categories, these diagnoses may actually confuse the field. Van Os and Tamminga suggest that *"Given the fact that we have not yet discovered the natural boundaries of psychosis, but only observe its properties, the only way to achieve progress is to periodically reassess all the evidence in the hope of catching a glimpse of its natural pathology".*[45]

There is also criticism regarding the dichotomy between affective and psychotic disorders. Craddock and Owen[46] argue that for almost 100 years, psychiatric research has been based on the assumption that schizophrenia and affective disorders are *"distinct entities with separate underlying disease processes and treatments"* and that this 'Kraepelinian dichotomy' is a core component of current classification systems. The fact that some individuals experience both prominent psychotic and affective symptoms questions the assumption of distinct diseases.[46] In a later publication, Craddock and Owen[47] stated that compelling evidence had come to light indicating that genetic susceptibility and genetic mechanisms are shared between psychotic disorders and affective disorders, and hence, the assumed dichotomous relationship between these disorders needs to be reconsidered.

Both of the points discussed above highlight the flawed nature of psychiatric diagnoses. These flaws lead to a lack of validity in diagnosis and in some cases, poor reliability and diagnostic misclassification. These issues must be borne in mind when conducting any research based around psychiatric diagnoses. However, the current diagnostic classification systems in use are the only things available to indicate that researchers and clinicians are referring to the same type of psychiatric disorder when they use diagnoses.

Bearing in mind the problems with current diagnoses discussed above, the alternative of diagnosis based on a continuum of symptoms, or even a continuum of psychosis, needs consideration. Craddock and Owen[46] have suggested that psychiatry need to move to a spectrum concept of diagnosis involving symptom dimensions. However, Lawrie et al.[48] argue that proponents of the continuum model of diagnosis offer this alternative to categorical diagnoses with no specific proposals, and also neglect to address the

potential limitations of such systems. Furthermore, the categorical diagnostic systems currently in use have evolved from clinical observation over long periods of time in order to aid treatment and prognosis, as well as to aid communication between clinicians but also researchers.[48]

It would potentially be possible to include cases who exhibit psychotic and depressive symptoms without using a categorical diagnostic system as an alternative to both categorical and continuum diagnostic systems. However, as mentioned above, the categorical systems currently in use are very useful for determining that different clinicians and researchers are examining and discussing the same clusters of symptoms within a patient, and are therefore likely to be examining the same disorder. This was part of the reason why such classification systems were created, to stop confusion about referring to potentially different disorders. Additionally, ICD diagnoses are currently used in clinical practice in the UK to diagnose patients. Therefore, to make this research relevant to clinical practice in the UK, and to be clear exactly what cluster of symptoms this thesis refers to, ICD diagnoses will be used.

2.7. Terms

Neki[2] describes how terms in psychiatry evolve over time and how through that evolution, confusion arises over the meaning. There have been certain periods in history when there has been no consensus on how schizoaffective disorder should be defined and diagnostic classification systems have openly acknowledged this (DSM-III,[19] RDC[13]). Historically, and even now, there is no consensus about whether schizoaffective disorder is a form of schizophrenia, a form of affective disorder or a separate entity.[49-51] DSM-III-R[19] highlights the fact that this term has had numerous meanings since it was first coined and introduced as a subtype of schizophrenia and

"represents one of the most confusing and controversial concepts in psychiatric nosology".[19]

A study by Brockington and Leff[31] suggested that agreement about the symptoms of schizoaffective disorder is low. They conducted a study comparing the definitions of schizoaffective disorder according to eight different diagnostic systems; ICD-8/9 (referred to as a hospital diagnosis in the paper); Catego system (Wing et al.[52]); Kendell's criteria (patient must fulfil stated criteria for schizophrenia or paranoid psychosis and depression or mania); Kasanin's description;[53] Stephens' criteria for good prognosis schizophrenia;[54] Welner's criteria;[55] Spitzer's research diagnostic criteria;[56] and a combination diagnosis (when a patient meets 1 of 10 definitions of schizophrenia and 1 of 9 definitions of manic or depressive psychosis). The authors found a mean mutual concordance of 0.19 and concluded that there is very poor agreement about the meaning of the term schizoaffective.

Similarly, PMD is known by various names; delusional depression; depressive psychosis; psychotic major depression; major depressive disorder with psychotic features. These names might all refer to the same disorder today, but as some point in the past, the term psychotic depression had a number of meanings including depression with severe impairment in functioning (section 2.2) and endogenous depression.[13] In 1959, Stengel[57] identified 38 different psychiatric classification systems and that was not even a complete survey.

This all highlights the importance of caution of comparing results between different classification systems and must be considered by anyone who is reviewing the literature in the area.

2.8. Diagnostic instability and implications for epidemiological studies

Diagnosis is subject to change over time. Symptoms may be minimal at first presentation and may emerge as the course of an illness develops. Sometimes symptoms are unclear and take time to develop. PMD and SAD are no exception to this and a number of studies have examined diagnostic stability over time. One follow-up of 15 years reported that 80% of participants with a diagnosis of PMD changed to bipolar at follow-up.[58] Therefore, it is important not only to look at baseline diagnosis in relation to risk factors and outcomes but also to look at follow-up diagnosis (this is further discussed in chapters 3 and 4).

2.9. Aims for the thesis

In light of the literature discussed above, the aims of this PhD thesis were:

1. To investigate the risk factors associated with PMD and SAD compared with other psychoses.
2. To investigate the long-term course and outcomes of PMD and SAD cases compared with other psychoses.

CHAPTER 3. Review of social adversity in the aetiology of PMD and SAD

"...if we wish to understand what keeps some societies healthy, yet others sick, we had better search among social facts for explanations."[59]

Kawachi and Berkman (2000)

3.1. Aims of the chapter

The aims of this chapter are to highlight the importance of psychosocial risk factors in the aetiology of psychosis and touch on the social concepts involved. This is followed by a review of the literature on social position and social experience risk factors for PMD and SAD, and a discussion of the methodological issues surrounding this literature. Finally, hypotheses leading from the literature are specified.

3.2. Introduction

As mentioned in chapter 2, an understanding of the risk factors involved in PMD and SAD could lead to better or faster recovery via effective interventions[34] or even prevention of disorder.[35] Risk factors in psychosis are commonly broken down into biological and psychosocial. Morgan et al.[60] state that the role of psychosocial aetiological factors are often down played, even when examined within a larger biopsychosocial model. This is despite many authors having highlighted the importance of the social environment, even in influencing biology,[61] with recent findings suggesting that social experiences can effect gene expression and neurodevelopment.[62] Bebbington et al.[63] state that there is a problem with physical and genetic explanations of psychosis as studies assume that all psychosis has a genetic origin based on the finding that some people with psychosis have a family history. There is also often an assumption that genetic aetiological factors lead to social factors and then disorder.[63] Bebbington et al.[63] also state that the way in which heritability is calculated is problematic because gene-environment interactions are counted in the genetic component of equations. These issues have led to renewed interest in the role of the psychosocial environment in the aetiology of psychoses.[62, 64]

There is strong evidence that social risk factors are important in the aetiology of psychosis. Bebbington et al.[63] point out that psychotic symptoms are related to representations of the social world making social experiences important. However, this importance of social factors in aetiology is important in treatment too. Various authors have highlighted the fact that they can be used to design interventions to promote behaviour change and social inclusion and have been used successfully.[59, 65, 66]

The majority of studies of risk factors in psychosis focus on schizophrenia and bipolar disorder.[67] Schizoaffective disorder is often included in the schizophrenia group or excluded from research all together. PMD is most commonly excluded from risk studies. This is highlighted in a short review by Smith et al.[68] who conclude that although risk factors for other psychotic disorders have been extensively examined, little research exists on risk factors for PMD. The authors also state that it is unclear whether risk factors for PMD overlap with those for depression and/or other psychotic disorders.

3.3. Review methodology

A scope of the literature using the very broad search terms of 'PMD/SAD' (and variations of) and 'social risk factors', indicated that there was very limited research on risk factors for PMD and SAD disorders (only two papers). Therefore, rather than conduct a very limited systematic review of social risk factors in PMD and SAD, a narrative review was conducted that included findings from related disorders, i.e. non-psychotic depression and psychosis in general. It was also possible to include findings on social risk factors in cases with a combination of psychotic and depressive symptoms but whom did not have a diagnosis of PMD or SAD. It was thought by the student that this research is relevant to creating sensible hypotheses.

3.4. Social concepts

Social research in mental health has many overlapping and connected concepts.[66] These include social disadvantage, social inclusion, social exclusion, social deprivation, social adversity, poverty, social experiences, social rejection, social isolation, social networks, social relationships, social capital, social processes, social integration and social fragmentation. The lack of definitions and use of numerous overlapping terms creates confusion about exactly what is being measured.[66] March et al.[69] state that social factors operate at many different levels: societies; regions; towns; neighbourhoods; families; and individuals. This thesis will focus on individual level risk factors.

Morgan et al. (2007) discuss the importance of distinguishing between direct and indirect risk factors. Therefore, within this review, individual social experiences have been divided into direct and indirect measures of social experience. Direct measures of social experience explicitly gather information about events and experiences individuals have had. They include childhood adversity and life events and difficulties. Indirect measures of social experience are proxies that indicate possible exposure to risk increasing experiences. These include sociodemographic characteristics, educational attainment, social isolation and employment.

This chapter will now outline the literature on individual level social experience in the aetiology of PMD and SAD.

3.5. Indirect markers of social experience

3.5.1. Sociodemographics

Turner et al.[70] suggest that certain sociodemographic characteristics affect mental health as they influence social experience and can lead to social adversity. Sociodemographic characteristics can include age, gender, ethnicity and social class / socioeconomic status.

Many studies have included PMD groups in their research and have reported on age, gender and more rarely, socioeconomic status. Several studies suggest that PMD is approximately twice as common in women than in men[25, 71, 72] (although one study found it was almost five times as common in women[73]). One review reported that the prevalence of PMD increases with age[68] while another stated that PMD is more common among people from lower socioeconomic classes.[74] However, much of the research has been based on samples which are not psychosis incidence samples, i.e. they have been either samples of cases in treatment (inpatients and outpatients) or only inpatients. Cases with a chronic course of illness and/or poor outcomes are more likely to be in contact with services and are therefore not necessarily representative of all PMD cases. Therefore, non-incident samples are likely to lead to biased estimates of associations with sociodemographic variables.

In 2004, Proctor et al.[27] examined first episode psychosis cases and reported an approximate even split of male and female cases with PMD (45% versus 55% respectively). They also reported more PMD cases in the 35-64 years age bracket compared with the non-affective psychoses (43% versus 30% respectively) and less cases in the 17-34 years age bracket (31% versus 48% respectively). However, these data were not central to the paper and the differences in sociodemographic variables between diagnoses were not examined statistically. Crebbin et al.[1] examined first

episode cases in northern England between 1998 and 2005. The authors reported that PMD was far more likely to occur in patients over 36 years old (RR=2.07, 95% CI=1.41, 3.04) whereas schizophrenia was more likely to occur in patients under 36 years (RR=1.56, 95% CI=1.01, 2.40). They reported that there were no differences in gender proportions in the PMD group but there was an interaction between age and gender with males under 36 years old being statistically significantly less likely (at $p < 0.05$) to have a diagnosis of PMD and males over 64 years being much more likely to have a diagnosis of PMD.[75] Women aged 36-64 were much more likely to be diagnosed with PMD than women in other age groups. Similar findings based on the same dataset were reported more recently.[76] These studies indicate that there may be a gender-age interaction in the risk of PMD. These studies are based on first episode psychosis incidence samples, thus attempt to be representative of all cases presenting to services. However, neither of these studies have accounted for diagnostic change, the importance of which is discussed below (section 3.8).

Baldwin et al.[77] examined the incidence of psychosis cases by gender using 6-month diagnosis. They reported an incidence of PMD in women of 7.4/100,000 population aged over 15 years compared with 5.4/100,000 for men. This is a stronger methodology as the authors were able to account for the potential diagnostic instability which is common in some psychotic diagnoses.[78]

Ethnic differences in the incidence of psychosis have been found[29] as well in specific psychotic symptoms in community samples.[79, 80] Fearon et al.[81]examined differences in incidence rates of different diagnoses by ethnicity in a first episode psychosis incidence sample. The authors reported that the incidence rate for PMD was elevated for all minority ethnic groups (African-Caribbean incidence rate ratio (IRR) 3.1, Black African

IRR 2.1, Asian IRR 3.0, Other IRR 5.6, Mixed IRR 4.0 and White Other IRR 1.3) compared with White British. This was in contrast to the pattern in schizophrenia and mania cases which had particularly raised rates in African-Caribbean individuals (IRR 9.1 for narrow schizophrenia and IRR 8.0 for manic psychosis), compared with rates for other ethnicities (narrow schizophrenia and manic psychoses: Black African IRR 5.8 and 6.2; Asian IRR 1.4 and 2.7; Other 3.5 and 3.0; Mixed IRR 2.6 and 6.2; and White Other IRR 2.5 and 1.7). This study is based on data from AESOP study which this thesis is based upon. In a systematic review and meta-analysis, Kirkbride et al.[29] reported that the rates of PMD were elevated in Black African and Black Caribbean migrants and their descendants compared with baseline populations. Although these studies on ethnicity have been conducted using first episode psychosis incidence samples, they have not taken account of diagnostic instability and therefore, may not provide accurate estimates of incidence of PMD. The relationship between ethnicity and psychoses is also closely linked to migration status. Migration status should also be examined in relation to the incidence of psychosis.[64]

Social class and socioeconomic status were not addressed in this thesis as unemployment and education were included which are markers of socio-economic status.

Previous research has found that "with increasing levels of urbanisation the incidence rates of psychosis and depression rose".[38] Although social context was not investigated here, the data in this thesis was collected from two centres which differed markedly by social context (see section 5.4), therefore, centre was included as a risk factor.

This section has demonstrated that although there are a handful of psychosis incidence studies on the social position risk factors involved in PMD, all but one of these have the methodological flaw that they have not accounted for diagnostic instability and therefore, may have produced biased findings (see section 3.8 for more details). Clearly, a study on the sociodemographic profile that indicates the social position in PMD and SAD cases is needed, that uses a psychosis incidence sample and accounts for diagnostic change. Based on the current literature, it was hypothesized that PMD and SAD would be associated with being of non-white British ethnicity, being female, being born outside the UK, being older and being in the London site.

3.5.2. Educational attainment

Education has been linked with various mental disorders, with reports of low educational attainment being associated with both psychosis[40] and depression[82] and having no formal qualifications being associated with affective psychoses (mix of PMD, mania and bipolar disorder cases).[83]

Sundquist et al.[38] explored the aetiological factors leading to first admission in a population based study in Sweden. They reported that a number of factors including low educational attainment were strongly associated with psychosis and depression, especially for men (Men: psychosis: hazard ratio 2.52 (95% CI 2.17-2.93); depression: hazard ratio 1.31 (95% CI 1.18-1.45); Women: psychosis: hazard ratio 1.85 (95% CI 1.62-2.10); depression: hazard ratio 1.45 (95% CI 1.33-1.58)). Although the authors examined first admissions rather than all incident psychosis cases which could have led to biased findings (only the most ill cases examined), it is impressive that they have included the whole population.

Morgan et al.[83] examined cumulative social adversity and isolation (defined using education, employment, living arrangements, housing, relationships and social networks) within the AESOP study in all incidence psychosis cases who presented to specialist mental health services in a defined period. The authors reported that affective cases were more likely to have no qualifications compared with controls (adjusted odds ratio 2.34, 95% CI 1.20–4.54). However, as this is affective psychoses, the sample is a mix of cases with PMD, mania and bipolar disorder, thus no conclusions can be drawn about PMD.

Morgan et al.[80] assessed the prevalence of psychotic-like experiences in a population based sample of healthy controls examining a range of social adversity markers and reported that in unadjusted analyses, having completed further education was significantly associated with having experienced psychotic-like experiences (unadjusted odds ratio 2.48, 95% CI 1.13–5.43) compared with those with higher education and those with only a school education or no education completed.

Only one study has examined educational attainment specifically within PMD or SAD. Jeste et al.[84] examined clinical and neuropsychological characteristics of PMD cases with schizophrenia and non-psychotic major depression cases and found no difference in the groups in terms of level of education. However, this was not an incidence psychosis sample and as previously discussed, this can lead to biased findings plus there was no healthy control group to make comparisons with. There was also no accounting for diagnostic change which could lead to inaccurate findings. This study was also a comparison between psychiatric diagnoses rather than a comparison with controls so nothing can be said about differences between PMD cases and the general population.

To learn about educational attainment as an aetiological factor in PMD and SAD, an incidence psychosis study is needed. As mentioned previously, a study which accounts for diagnostic change would be advantageous as well as one that compares the cases to a control group representative of the general population. Based on the literature discussed above, it was hypothesized that lower educational attainment would be more frequent in PMD and SAD cases compared with controls.

3.5.3. Social Isolation

Berkman and Glass[85] discuss how Cassel[86] and Cobb[87] were the first to suggest a link between social isolation (lack of social resources and social support) and disease risk. The mechanisms by which social networks might influence disease patterns and the way they operate are discussed by Berkman and Glass[85] but are beyond the scope of what was feasible in this thesis and so are not covered here. The authors discuss the complex ways of defining social networks; e.g. range/size; density; boundedness; homogeneity; frequency of contact; multiplexity; duration; and reciprocity. However, in order to keep this review as broad as possible and to inform future research, social isolation was broadly defined as any experience which could lead to reduced social contacts, social resources and social support.

A number of studies have explored social isolation as a risk factor for mental disorder including psychosis and depression. Sundquist et al.[38] examined living alone compared with cohabiting/married as risk factors for first admission in their population based study in Sweden. The authors reported that living alone was strongly associated with psychosis and depression in women (psychosis hazard ratio 3.23 (95% CI 2.98-3.49); depression hazard ratio 1.66 (95% CI 1.58-1.75)), but especially so for men (psychosis hazard ratio 6.02 (95% CI 5.45-6.64); depression hazard ratio 1.93 (95% CI 1.81-

2.05)).[38] Drukker et al.[40] conducted a study in the Netherlands examining indicators of social adversity in first episode schizophrenia cases compared with controls. They reported that being divorced, single or widowed were associated with higher risk of treated psychotic disorder (OR 71.95, 95% CI 22.42-230.95; OR 46.39, 95% CI 9.63-223.39; OR 41.22, 95% CI 7.87-215.98 respectively) but living alone or with non-family was associated with a reduced risk of treated psychotic disorder (OR 0.14, 95% CI 0.05-0.40; OR 0.42, 0.11-1.60 respectively).[40]

Within the AESOP study, several papers have examined social isolation within a sample of all first episode psychosis cases who presented to services in a defined period. Morgan et al.[88] examined individual indicators of social isolation and reported that the following factors were associated with the 'all psychoses' group: having no close confidants (OR 7.8, 95% CI 4.9-12.5), never having a long-term relationship (OR 4.0, 95% CI 2.9-5.7) and having been unemployed for more than a year (OR 2.0, 95% CI 1.5-2.6). Morgan et al.[83] examined cumulative social isolation within the concept of 'social adversity and isolation' defined by using data on education, employment, living arrangements, housing, relationships and social networks. The authors reported that in the affective cases, the following social isolation factors had significantly higher odds ratios: being currently unemployed (adjusted OR 2.56, 95% CI 1.56-4.20); living alone or with relatives (adjusted OR 2.09, 95% CI 1.28-3.40; adjusted OR 4.45, 95% CI 2.18-9.07 respectively); being single (adjusted OR 2.04, 95% CI 1.31-3.16); never having had a long-term relationship (adjusted OR 2.61, 95% CI 1.57-4.34); having contact with friends less than daily (adjusted OR (weekly contact) 2.56, 95% CI 1.49-4.39; adjusted OR (less than weekly contact) 3.62, 95% CI 1.97-6.66); and having no close confidants (adjusted OR 5.20, 95% CI 2.85-9.49). Within the same sample, Reininghaus et al.[89] reported that the odds of being a case increased as levels of social contacts decreased

and that non-affective psychosis cases were more likely to experience lower levels of social contacts (low versus high social contacts, unadjusted OR 3.01, 95% CI 1.64–5.52; medium versus high social contacts, unadjusted OR 1.85, 95% CI 1.04–3.26) but this was not true for affective psychosis cases (low versus high social contacts, unadjusted OR 1.67, 95% CI 0.84–3.32; medium versus high social contacts, unadjusted OR 1.14, 95% CI 0.61–2.15).

Morgan et al.[80] further examined the association between social isolation and psychotic-like experiences in a healthy population. They reported that never having been in a long-term relationship was associated with psychotic-like experiences (unadjusted OR 1.85, 95% CI 1.02–2.39) but there was no association for having no close confidants, and having infrequent contact with friends and/or family.

None of the papers on social isolation have specifically examined PMD or SAD as these diagnoses have been excluded or amalgamated into larger diagnostic groups. Therefore, no conclusions can be drawn about PMD or SAD and clearly further research on social isolation as a risk for PMD and SAD is needed. Based on the above literature, it was hypothesized that factors associated with social isolation, such as living situation, relationship status and contact with friends, would be more frequent in PMD and SAD cases compared with controls.

3.5.4. Employment

As suggested above, employment could be conceptualised within social isolation but it is also an important factor in itself. The link between unemployment and health, mental health and wellbeing has been well documented.[90-92] Warner highlights the importance of employment as increasing income, expanding social support and bringing a sense of

meaning to life with unemployment bringing alienation and isolation.[93] Kasl and Jones in their review of the area state that "unemployment clearly increases psychological distress, particularly symptoms of depression...".[90]

A number of studies have found a link between psychosis and unemployment. Drukker et al.[40] conducted a study in the Netherlands examining neighbourhood and individual level indicators of social adversity in schizophrenia cases compared with controls. Specifically for employment they reported that unemployment was associated with a higher risk of treated psychotic disorder (OR 11.13, 95% CI 6.62-18.72). Importantly the authors acknowledge that they were examining treated psychosis only. As mentioned above, the AESOP study (first episode psychosis study) has reported that, in their sample, current unemployment (adjusted OR 3.61, 95% CI 2.19–5.96) and being unemployed for 1 year or more (adjusted OR 2.44, 95% CI 1.40–4.25) were both associated with psychosis in general whereas only current unemployment was associated with affective psychosis at $p < 0.05$ (adjusted OR 2.56, 95% CI 1.56–4.20).[83]

Some of these studies included PMD and SAD cases but no study has examined employment in the aetiology of PMD or SAD specifically. However, one study by Shevlin et al. examined symptoms rather than diagnoses and reported that the odds ratio of having experienced visual hallucinations was decreased for those who were working at the time of interview (OR 0.57, 95% CI 0.34-0.95).[79] Morgan et al.[80] assessed the prevalence of psychotic-like experiences in a population based sample of healthy controls examining a range of social adversity markers including current and long-term (1+ year) unemployment. They reported that both definitions of unemployment were not associated with having experienced psychotic-like experiences.

No study has examined employment in the aetiology of PMD and SAD. As unemployment is a risk factor for psychosis in general as well as for affective psychosis, and as unemployment has been linked with depression, it was hypothesized that unemployment would be more frequent in PMD and SAD cases compared with controls. In order to test this hypothesis, and overcome key methodological limitations of other research, a study of incidence psychosis PMD and SAD cases was needed and as previously mentioned, one which accounts for diagnostic change.

3.6. Direct measures of social experience

Direct measures of adverse social experience included in this thesis are childhood adversity and life events and difficulties pre onset of psychosis.

3.6.1. Childhood adversity

3.6.1.1. Definitions and importance

Childhood adversity is a term used to capture a variety of negative experiences that have occurred in childhood. These include, but are not restricted to, physical abuse, sexual abuse, emotional abuse, neglect and separation from parents. Within the review of the literature for this thesis, the term childhood adversity has been used in the broadest sense of the term so as not to miss any relevant literature.

Hill[37] highlights the importance of studying childhood adversity as this will "...help to clarify heterogeneity and provide pointers to mechanisms based on different developmental pathways". As well as helping to understand the possible causes of psychosis, identifying patients with experience of childhood adversity may reveal different treatment needs of patients.[37] This may lead to the potential for creating more

effective treatments and preventive strategies as well as predict treatment responses.[37] Bernet and Stein[94] identified that certain types of abuse predict course of depressive illness, thus identifying childhood adversity in PMD may also be useful in terms of prognosis.

3.6.1.2. PMD, SAD and childhood adversity

A large number of studies have been conducted on the link between childhood adversity and mental illness. However, only a single study has been conducted on the role of childhood adversity in the aetiology of PMD or SAD. Other studies have included PMD[95] or SAD cases[96-98] but these cases are amalgamated into broader diagnostic groups such as schizophrenia broadly defined or 'psychosis', severely limiting the conclusions about PMD/SAD and childhood adversity.

However, studies on childhood adversity as an aetiological factor in non-psychotic depression and general psychosis are relevant to PMD and SAD as they are a combination of the two symptoms clusters. These studies may be able to inform hypotheses on childhood adversity as a risk factor for PMD and SAD.

3.6.1.3. Depression

It has long been recognised that childhood adversity is a risk factor for depression..[41] In his review in 2006, Hill[37] stated that studies reporting an association between child maltreatment and adult depression have been remarkably consistent in their findings of a positive association. Hill discusses some of the earliest studies examining depression and childhood adversity which focussed on loss of a parent. However, childhood adversity goes far beyond this and a number of different types of childhood adversity have been associated with depression. As well as parental loss[99-102], studies have

examined sexual abuse,[103-109] physical abuse,[94, 108, 109] emotional abuse,[94] neglect[94, 109] and often a combination of these.[107-109]

Childhood sexual abuse (CSA) and its role in the aetiology of depression has been a major area of research. CSA has been consistently associated with a diagnosis of depression in adulthood.[103, 104, 108, 110, 111] A systematic review and meta-analysis of 17 case control studies and 20 cohort studies reported that there was a significant association between CSA and depression (OR 2.66, 95% CI 2.14-3.30) regardless of gender or age at which the abuse occurred.[112]

Bifulco et al.[106] examined CSA and depression in a sample of women over a two year period. More women who had experienced CSA had depression during the period (64%) compared with those with no experience of CSA (26%). The authors also found that CSA was associated with other early stressful experiences such as parental indifference, violence and institutional stay. This finding highlights the importance of examining multiple types of childhood adversity as adversities are often associated with each other.

Many studies have examined multiple types of childhood adversity within the same study. Young et al.[105] examined childhood adversity which they defined as emotional, physical or sexual abuse. They found that childhood adversity was extremely common in patients with mood disorder, however, there was no control group for comparison. Kessler et al.[113] examined occurrence of mental disorders in a household population survey comparing those who had experienced childhood adversity with those who had not. Childhood adversity was defined as loss events (death, separation from parents or parental divorce/separation), parental psychopathology (depression, anxiety,

drug/alcohol use, antisocial personality disorder), interpersonal traumas (sexual or physical abuse, aggression, kidnapping) and other adversity (accident, natural / manmade disasters, witnessed trauma, other post-traumatic stress disorder events, shocked)). The authors reported that overall adversity was associated with a range of disorders including depression. Bernet and Stein[94] examined childhood trauma retrospectively among a cohort of depressed outpatients compared with a control group. They reported that depressed cases had higher scores on the Childhood Trauma Questionnaire (CTQ) which covers sexual abuse, physical abuse, emotional abuse, physical neglect and emotional neglect. Depressed cases also scored higher on the emotional and physical abuse subscales as well as on the emotional neglect subscales, but not on the physical neglect and sexual abuse subscales.

One of the most recent studies on depression and childhood adversity is by Wingenfeld et al.[114] They examined childhood adversity, adulthood adversity and stress in the previous year in a sample of inpatients with major depressive disorder compared with patients with borderline personality disorder and controls. They assessed childhood adversity using the Early Trauma Inventory[115] which is a semi-structured interview that includes general trauma, physical abuse, sexual abuse and emotional abuse. The authors reported that the depressed patients scored significantly higher on the general trauma, physical abuse and emotional abuse sections of the early trauma inventory compared with controls but not on the sexual abuse section. Depressed cases also scored higher on the Trauma Assessment for Adults.[116] The authors stated that regression analyses revealed that depressive symptoms were predicted by emotional abuse in childhood and violent experiences in adulthood. The finding that childhood and adulthood depression is associated with depression has also been reported by Kendler et al.[117] in their population-based sample of women. The authors reported that onset of depression was

best predicted by childhood sexual abuse, severe life events and neuroticism. The authors further found that cases who had experienced childhood sexual abuse had an increased sensitivity to severe life events. These two studies highlight the importance of studying both life events and childhood adversity simultaneously. In fact, the finding that life events and childhood adversity are associated in patients with depression or depressive symptoms is not a new finding with various studies having found this association in a variety of settings including women presenting to an emergency room and women from primary care settings.[118-120]

3.6.1.4. Psychosis

In 2009, a review of the literature by Manning and Stickley[41] highlighted that a number of studies have found an association between childhood abuse and a range of mental illnesses including psychosis. The authors' key findings were that "a significant proportion of people appear to develop psychosis following all types of childhood abuse". They also stated that positive symptoms of psychosis appeared to be the most strongly correlated with childhood abuse. Schafer & Fisher[121] reviewed the evidence for an association between childhood adversity and psychosis in population-based studies. They concluded that "the evidence for an association between childhood trauma and psychosis is steadily accumulating" and go on to state that this is further supported by studies which have found a 'dose response' relationship.

Some studies have found the association between childhood adversity and psychosis to be present for only certain types of adversity. Shevlin et al.[97] investigated childhood rape, serious assault, physical abuse, neglect and sexual molestation using data from an epidemiological population survey. They reported that only physical abuse predicted psychosis in later life. They also reported that childhood rape was predictive of

psychosis in male cases only. Thus, serious assault, neglect and sexual molestation were not found to be associated with psychosis in this study.

Some studies have even found a lack of association between psychosis and childhood adversity. Spataro et al.[110] used a data linkage design to examine the link between childhood sexual abuse and mental health, innovatively using records of medical examination that confirmed abuse and linking this to mental health treatment records. They included both male and female cases and reported that there was no increased relative risk for schizophrenic disorders in those with a history of CSA. An extension of this study was performed and reported by Cutajar et al.[103] Information on abuse confirmed by a medical examiner was extracted from medical records and was again linked to psychiatric records to create a 12-43 year follow-up. The authors reported that exposure to CSA did increase risk for a variety of disorders including psychosis (OR 2.13, 95% CI 1.44–3.17). The systematic review and meta-analysis by Chen et al.[112] which included 3,162,318 participants with a range of psychiatric disorders reported that there was no statistically significant association between CSA and schizophrenia.

Bebbington et al.[122] investigated lifetime victimisation experiences in a population sample examining participants with a probable psychosis, a current neurotic disorder, an alcohol dependence or a drug dependence. The authors reported that participants with a probable psychosis had an increased odds (compared with no disorder controls) of having experienced sexual abuse (OR 15.47, 95% CI 8.2-29.2), bullying (OR 4.24, 95% CI 2.3-7.8), being taken into care (OR 10.71, 95% CI 5.2-22.0), violence at home (OR 8.97, 95% CI 4.8-16.6), running away from home (OR 11.49, 95% CI 6.2-21.2), time in a children's institution (OR 11.87, 95% CI 6.1-23.2), homelessness (OR 11.34, 95% CI 6.0-21.3), being victim of a serious injury, illness or assault (OR 5.21, 95% CI 3.0-9.1)

and violence at work (OR 3.66, 95% CI 1.4-9.5) but not expulsion from school (OR 0.88, 95% CI 0.1-6.3). The probable psychosis group had a higher odds ratio on all these variables compared with participants with a common mental disorder or drug / alcohol dependence except on expulsion from school. However, when clustering of victimisation experiences was controlled for, only six of the risk factors remained statistically significant and the odds ratios for all experiences were reduced. This demonstrates the importance of examining multiple types of childhood adversity due to their interaction. One of the problems with this study, however, was that the experiences investigated occurred at an unspecified time in the participants' lives. Some of the experiences can be assumed from the nature of the event (e.g. being expelled from school) but not for others (e.g. being homeless). Bebbington et al.[122] also found that lifetime victimisation experiences co-occurred which may be due to early adversity predisposing to later adverse events which they called a "clustering of disadvantage". This highlights the importance of examining both childhood adversity and life events together.

Morgan and Fisher[123] in their critical review of the area, highlight the issues with research on the link between psychosis and childhood trauma. They point out that most studies focus on small samples of heterogeneous and chronically ill samples and stress that this is not informative about the aetiological role of childhood adversity in psychosis. The authors point out that differences between studies in the definition and measurement of trauma makes comparisons difficult and may explain the variation in findings. Morgan and Fisher advise caution in the over interpretation of findings from childhood trauma and psychosis due to the literature being inconsistent and the many methodological limitations the studies contain.[123]

3.6.1.5. Symptoms not diagnoses

From the above literature, it appears that the association between childhood adversity and depression is well established. However, the association between childhood adversity and psychosis is a little less certain. This makes it difficult to hypothesize what the relationship between PMD/SAD and childhood adversity might be. However, studies examining psychotic symptoms rather than specific diagnoses might be more helpful due to issues surrounding diagnostic classification (see Chapter 2).

Several studies have examined the relationship between psychotic experiences and childhood adversity. As part of a prospective study of the incidence of mental illness in the Netherlands, Janssen et al.[124] assessed childhood abuse using a semi-structured interview which assessed emotional, physical, psychological and sexual abuse before the age of 16 years old. The authors reported that childhood abuse was associated with: Brief Psychiatric Rating Scale (BPRS) any psychosis (any rating of over 1 on the BPRS items 'unusual thought content' and 'hallucinations'); and BPRS pathology level of psychosis (any rating of over 3 on the BPRS items 'unusual thought content' and 'hallucinations'). After controlling for various sociodemographic and clinical variables plus urbanicity, the odds ratios of experiencing psychosis in the presence of a history of child abuse reduced from 11.5 (95% CI 2.6–51.6) to 7.3 (95% CI 1.1–49.0) but remained statistically significant. Further analysis of multiple adversities revealed a dose response relationship between number of types of abuse and both outcomes.

Whitfield et al.[125] examined the relationship between multiple adverse childhood experiences and hallucinations in a sample of participants who were members of a health maintenance organization in the US. The adverse childhood experiences included were: emotional abuse; physical abuse; sexual abuse; battered mother; household

substance abuse; mental illness in household; parental separation or divorce; or incarcerated household member. The authors reported that the risk of hallucinations were increased 1.2- to 2.5-fold by any adversity (although the incarcerated household member item had a CI which crossed zero and therefore would not be statistically significant). The authors also reported a graded relationship between number of different types of adversities and history of hallucinations.

Shevlin et al.[79] conducted a study similar to Whitfield et al. but they only included childhood physical assault, rape and sexual assault. This was part of a national epidemiological survey in the US. The authors reported that rape, sexual assault and physical assault were associated with both auditory and visual hallucinations. When the authors adjusted for multiple adversity and demographic variables, the relationship between physical assault and rape with visual and auditory hallucinations remained (physical assault: visual hallucinations OR 3.22 (95% CI 1.46–7.09); auditory hallucinations OR 4.55 (95% CI 1.96–10.57)); rape: visual hallucinations OR 3.41 (95% CI 1.72–6.76); auditory hallucinations OR 2.97 (95% CI 1.39–6.33)) but the relationship of both types of hallucinations and other sexual assault became non-statistically significant (visual hallucinations OR 1.57 (95% CI 0.80–3.06); auditory hallucinations OR 0.73 (95% CI 0.32–1.64)). The authors also examined multiple adversity and reported that cases with one adverse experience were almost three times more likely to experience visual hallucinations whereas those who experienced two adverse experiences were almost six times more likely to experience visual hallucinations, and almost 14 times for those who experienced three types. This indicates a dose response relationship in visual hallucinations.

Several studies have even examined psychotic symptoms in children with adverse experiences. Studies have reported various types of trauma are positively associated with clinical and non-clinical psychotic symptoms in childhood and adolescence.[126-128] Dose-response relationships were also found.[126-128]

This section has demonstrated that psychotic experiences which are experienced in PMD and SAD are associated with childhood adversity.

3.6.1.6. Depression and Psychosis

The studies mentioned above, examine depression and psychosis as separate entities. However, in PMD and SAD, there is a mixture of depressive and psychotic symptoms. Therefore, studies which examine the interaction between psychotic and depressive symptoms may be informative.

Offen et al.[95] examined depressive symptoms in a sample of patients with psychotic disorders (mostly schizophrenia) involving auditory hallucinations. The authors reported that a history of child sexual abuse in these patients was associated with a higher level of depression. The study by Bebbington et al.[122] (mentioned above) in which a range of victimisation experiences were elevated in probable psychosis cases compared with no disorder controls also found that when controlling for depression the odds ratios decreased but remained significant for all items except bullying, being taken into care, violence at home and violence at work. The authors interpret this as depression attenuating the relationship between psychosis and those experiences.

Schenkel et al.[96] investigated childhood maltreatment (defined as physical abuse, sexual abuse and neglect) in psychiatric inpatients with a schizophrenia spectrum disorder. The

authors reported that patients with a history of childhood maltreatment were more likely to have elevated symptoms of depression on the BPRS. A further study by Bebbington et al.[129] used a general population sample to explore the relationship between childhood sexual abuse and psychosis. They identified potential psychotic cases by using the Psychosis Screening questionnaire and asking about participants having a diagnosis of psychosis, being on antipsychotics or having been admitted for mental health problems. Anyone who was positive for any of these were then interviewed using the Schedules for Clinical Assessment in Neuropsychiatry. Interestingly, when controlling for depression the odds ratios decreased from 3.5 to 2.3 (95% CI 1.2–4.1) but remained statistically significant. This led the authors to conclude that although depressed mood did attenuate the relationship between psychosis and victimisation experiences, that relationship was still independent of depressed mood.

3.6.1.7. PMD

Only one study has examined the association between PMD and childhood adversity. This was conducted by Fisher[130] who reported on data from the AESOP first episode psychosis study. Fisher reported on severe childhood maternal physical abuse, childhood maternal separation and childhood sexual abuse and found an odds ratio of 3.81 (95% CI 1.07-13.60), 1.97 (95% CI 0.78-4.97) and 1.82 (95% CI 0.56-5.91) respectively. When this analysis was adjusted for potential confounding variables (gender, age at interview, ethnicity, study centre and parental social class), these odds ratios became 1.94 (95% CI 0.30-12.67) for maternal physical abuse, 1.08 (95% CI 0.31-3.70) for maternal separation and 1.99 (95% CI 0.51-7.79) for sexual abuse, with none remaining statistically significant. There is no analysis of overall childhood adversity and its association with PMD or with number of types of different adversity. There is also no accounting for diagnostic stability.

3.6.1.8. Summary of childhood adversity

The literature reviewed in this chapter suggests that there is an association between childhood adversity and both depression and psychosis, both of which are major components of PMD and SAD. A link between childhood adversity and specific depressive and psychotic symptoms has also been supported. This led to the hypothesis that childhood adversity would be more frequent in PMD and SAD cases compared with controls.

3.6.2. Life events and life difficulties

3.6.2.1. Definitions and importance

Life events have been viewed and defined in a number of different ways. Dohrenwend and Dohrenwend[131] defined life events as "stressful stimuli or situations to which everyone is exposed to a greater or lesser extent in the natural course of life". Brown and Harris[36] view life-events in terms of the emotions they arouse and highlight the importance of the meaning of events rather than the events themselves. Brown[132] states that life events have become a useful way to explore stress and explore whether stress is an internal response to external events or whether it is the external event itself. Brown[132] highlights that although life events do not mean anything to the person until they have translated it, life events do exist independently of any such translation.

Life events have been referred to in a number of different ways: 'life stress';[133] 'severe events and major difficulties';[134] 'victimization experiences and traumatic events';[135] 'trauma';[136] 'stressful life events';[137] 'traumatic events';[138] 'chronic and acute stress';[139] and 'psychosocial stress'[140] among others. Within this review, life events were considered as broadly as possible in order to not miss any relevant research in the area.

The importance of examining life events and difficulties was highlight by Turner et al.[70] as there is the potential for targeting stressful events and life circumstances as part of future prevention strategies. Therefore, understanding the distribution of these factors and their interaction with other risk factors is important.

3.6.2.2. Depression

Evidence demonstrating a relationship between stressful life events and the onset of mental illness, especially depression, has been steadily accumulating.[140] A thorough exploration of the historical research that has led to current understandings about life events and mental illness are given by Dohrenwend and Dohrenwend[141] and Lloyd[140], and this is not repeated here. However, it is worth mentioning one of the first studies to examine depression specifically by Paykel et al.[142] in 1969. Paykel et al.[142] studied depressed patients who were a combination of inpatients and outpatients and compared these with controls recruited as part of an epidemiological community survey. They used a life events list which covered 6-months prior to onset. The study revealed that patients reported almost three times as many events as controls. This was the first study to use general population controls thus improving on previous work.

In a landmark study, Brown and Harris[36] identified the 'contextual threat' of life events as the important aetiological factor in depression rather that the life event itself. The authors conducted interviews with working class women in London focussing on life events and ongoing difficulties. The authors were able to improve on previous research on life events by rating the level of threat that most people would experience in a similar situation to stop the problem of subjective interpretation of life events. This study confirmed previous findings of a relationship between life events and depression while using a less subjective methodology. They also demonstrated that loss, entrapment and

humiliation are particularly important and the six month period pre-onset is the salient time period.

In their literature review, Brown and Harris,[143] discuss research from two types of study sample which replicate the original study by Brown and Harris.[36] The first study sample involved population based studies conducted over a variety of time periods, in a variety of settings, with a variety of different populations. Nine studies based on this sample reported that severe events or major difficulties were much more common in the period before onset in depressed patients compared with controls. Severe events or major difficulties occurred in 25-39% of controls compared with 62-94% of cases.[143] The second type of study sample involved examining life events and onset of depression in psychiatric patients. Eleven studies reported that 18-73% of cases experienced at least one event compared with 8-30% in the control groups.[143] These studies therefore demonstrated that the association between life events and depression exists in more than one setting.

Kendler et al.[144] examined stressful life events in a population based twin study in the US. High threat severe life events were documented using the LEDS and loss, humiliation, entrapment and danger were specifically selected and rated. High ratings of loss and humiliation predicted onset of major depression as did the loss subcategories of death and respondent-initiated separation. The combination of humiliation and loss events was more 'depressogenic' than pure loss (even than death). The authors concluded that "in addition to loss, humiliating events that directly devalue an individual in a core role were strongly linked to risk for depressive episodes".

Some studies have looked at depressive symptoms rather than a diagnosis of clinical depression. McGonagle et al.[139] examined acute and chronic stressors and depressive symptoms in a community survey of married men and women in Detroit. Depressive symptoms were measured using the Hopkins Symptom Checklist and included a period of only 30 days prior to interview. Chronic and acute stress over the 12 months prior to interview were measured using questions from lists compiled by Brown and Harris[145] and Dohrenwend, Krasnoff, Askenasy and Dohrenwend.[146] A chronic stress was defined as a stress that started more than 12 months before the interview. An acute stress was defined as a stress that started within 12 months of the interview. All point-in-time events were coded as acute stressors. The authors found that both acute and chronic stress were associated with depressive symptoms in both men and women. The authors conclude that chronic stressors were more strongly associated with depressive symptoms than acute stressors in all (physical illness, marital conflict and interpersonal conflict) but one life domain (financial difficulty).

Turner et al.[70] examined the relationship between social stress (life events and life difficulties) and depressive symptoms as well as depressive disorder. This was done within the context of a population based study of residents of Toronto. They measured stressful life events using a 34-item checklist and chronic stressors using a 51-item inventory. The authors reported that recent life events and chronic stress were both correlated with depressive symptoms and major depressive disorder.

Many studies have also examined the relationship between life events and depression within the context of other risk factors. Turner et al.,[70] for example, examined the influence of social statuses (age, gender, marital status and occupation). They reported a

clear association between life events and sex, age, marital status and occupational status.

As mentioned above, a number of studies have examined the interaction of life events and childhood adversity on depression and found a relationship between these two risk factors.[117, 147] Briere et al.[119] examined overall psychiatric problems in women presenting to an emergency room. The authors reported that child and adult victimizations were intercorrelated and that both were uniquely associated with psychiatric difficulties, even after controlling for other relevant factors. They found that three clinical variables including depressive disorder was associated with having been battered within a sexual relationship.

3.6.2.3. Psychosis

One of the earliest studies on the link between life events and psychosis was by Brown and Birley.[39] The authors investigated the rate of crises and life changes in the 12 weeks prior to onset of schizophrenia (split into four 3-week periods) compared with a non-ill comparison group. Case notes of all patients admitted to hospital in a defined area were examined and any patients who might have had schizophrenia were interviewed. The researchers went through a list of events which (based on common sense) were thought to be likely to produce an emotional disturbance in most people. Events involved danger; significant changes in health, status or way of life; the potential for significant changes in health, status or way of life; and important disappointments. The authors reported that the patient group had more life events, independent life events and possibly independent life events compared with the controls in the 3 week period closest to onset, but not in the other 3-week periods prior to and further away from onset. The authors interpret the findings as evidence that environmental factors can precipitate an

episode but state that life events are not a sufficient cause. The authors suggest that *"...a number of factors must contribute and perhaps coincide to produce the conditions necessary for an acute schizophrenic attack..."*.[39] The investigation of independent life events here is an important methodological advance.[148] This is because events which are a consequence of illness rather than a cause, will lead to mistaking direction of causation.

In his review of the area, Day[149] stated that if we evaluate the evidence "...we find that a substantial majority of all the relevant studies in this area have produced findings that, although less than definitive, still support the existence of a causal association between stressful life events and the acute onset of positive symptoms in schizophrenic patients". He goes on to state that there are no more than a handful of studies which report negative findings,[149] although it is important to remember that negative findings are less likely to get published.[150] Day points out that although an association has been identified between schizophrenia and life events in a variety of studies, this does not necessarily mean a causal link. However, the alternative explanations of an artifactual association or indirect association is questioned by Day who claims that researchers' careful attention to the issue of temporal sequence in life events rules it out and he concludes that the association between stressful life events and episodes of schizophrenia are probably causal.

Work on life events and psychosis has also been conducted more recently. As mentioned in the childhood adversity section, Bebbington et al.[122] investigated lifetime victimisation experiences in a population sample. Although the experiences investigated occurred at unspecified times in the participant's lives, one of the experiences is much more likely to have been in adulthood – violence at work. On this item, the probable

psychotic disorder group had an odds ratio of 3.66 (95% CI 1.4-9.5) compared with controls. However, when clustering was controlled for, this reduced to an odds ratio of 1.22 (95% CI 0.4-3.6, p=0.72).

Some researchers have even examined life events and psychotic symptoms. Newman et al.[151] examined victimization and traumatic experiences in consecutive admissions of patients with schizophrenia and schizoaffective disorder using the stressful life events screening questionnaire. Victimization was defined as incidents that were of a violent and interpersonal nature and involved a perpetrator. Traumatic experiences were defined as non-interpersonal incidents, events without a perpetrator, e.g. natural disasters or motor vehicle accidents. There was evidence of associations between traumatic events and PANSS positive symptoms (beta coefficient of 0.92), PANSS cognitive/autistic symptoms (beta coefficient of 0.89) but not with the PANSS dysphoric symptoms. The authors reported that non-interpersonal traumatic experiences were associated with severity of psychosis and concluded that "past traumatic and victimisation experiences are significantly associated with schizophrenia patients' symptom severity".

Despite these positive findings it should be borne in mind that findings on the hypothesis that life events trigger onset or relapse of schizophrenia are mixed and that the retrospective nature of most of the studies questions the validity of the findings.[152] However, due to the nature of the exposure and the rarity of the outcomes, prospective studies of life events and psychosis are not feasible.

3.6.2.4. PMD and SAD

Studies have included SAD cases as part of a broader diagnostic group,[153, 154] but none have reported on SAD separately from other diagnoses. However, studies on life events in PMD have been conducted.

A paper by Brown et al.[134] examined life events and difficulties in psychotic and neurotic depressed patients. However, there is no mention of the diagnostic classification system that was used in this study. Chapter 2 discusses issues surrounding the use of the term 'psychotic depression' to refer to severity of depression not depression with psychotic features. Considering the era that this paper is from and the fact the authors compared the group to 'neurotic' depression patients, it is highly unlikely that the psychotic depressed group are what we would refer to as PMD. Therefore, this paper is not necessarily relevant to this discussion.

Other studies have looked at the role of life events in PMD as would be defined today. A study by Samuel and Varghese in 2003[155] randomly selected a sample of 30 patients with PMD from an outpatient clinical in India. They found that precipitating factors in the form of life events were reported in 53% of patients. These events included recent marriage, job loss and residential upheaval. Unfortunately, the authors did not include a control group and 60% of the PMD cases had a history of bipolar disorder, bringing into question whether they were actually PMD cases at all. This was the only publication based on this study (personal correspondence with authors).

Bebbington et al.[156] examined patients hospitalised for psychotic disorders in the UK. They found that 10/14 (71.4%) of patients with PMD reported moderate/severe life events (independent and possibly independent) in the three months prior to onset of the

index episode. This is compared with 51.9%, 45.2% and 10.1% for the schizophrenia, mania and control groups respectively. When examining independent moderate/severe events only, 50% of PMD cases were positive for having experienced these events compared with 34.6%, 25.8% and 7.2% for the schizophrenia, mania and control groups respectively. Whether examining life events which were moderate/severe or mild and examining 3 months before the onset of the disorder or four to six months before the disorder, the PMD consistently had higher proportions of cases who experienced life events compared with the other three groups (except independent mild events at four to six months). These findings indicated that life events were more highly associated with PMD compared with schizophrenia and psychotic mania. However, the study only examined inpatients so arguably focussed on the more severely ill cases of psychosis. The sample also only included 35 out of 97 cases who were first episode. Therefore, the findings are mostly relevant for life events as a risk factor for admission rather than as a risk factor for onset of the disorder. To answer the question of whether life events and difficulties are risk factors for the onset of PMD, a study examining first episode inpatients and outpatients needs to be conducted.

3.6.2.5. Summary of life events and difficulties

Van Os et al.[157] argued that "The associations between life events and illness onset is not specific to any particular diagnostic category within the functional psychoses, but there is some evidence that the effect sizes are greater in affective illness than in schizophrenia". Based on this and the literature above, it was hypothesized that independent life events would be more frequent in PMD and SAD cases in the year prior to illness onset compared with controls.

3.7. Family history of psychosis

Genetics clearly play an important part in the aetiology of psychosis.[158] Although this thesis is concerned with the psychosocial risk factors involved in PMD and SAD it would be foolhardy to ignore the role of genetics completely. In fact, studies have found that there are interactions between genetics and various psychosocial factors in psychosis and depression (e.g. childhood adversity[130] and life events[159]). Therefore, although this thesis is concerned with the psychosocial risk factors involved in PMD and SAD, the analyses will include a measure of family history of psychosis / mental illness. However, there will be no way to determine if this family history indicates the aetiological importance of genetics or environment.

3.8. Methodological issues

This review has picked up upon some key methodological challenges in studies on the aetiology of psychoses which have not been addressed by previous research on PMD and SAD cases. Firstly, PMD and SAD cases are often amalgamated into other diagnostic groups meaning that no conclusions can be drawn about the aetiology of PMD and SAD cases.

Secondly, diagnostic stability is something that is rarely, if ever, considered in studies of risk factors. Schwartz et al.[160] stated that "… the psychiatric diagnoses people receive at the time of onset are often inaccurate..." and the authors therefore recommend that longitudinal studies are needed to clarify the nature of the patient's illness. In studies which only examine baseline diagnosis in relation to risk factors, the findings could be inaccurate especially in relation to PMD and SAD which have low diagnostic stability (further discussed in section 4.4.2.1).

Finally, there is the issue of sampling. The majority of studies on risk factors are based on non-first episode illness samples. Within this thesis, incidence samples (all new cases of first episode psychosis in a given area) have been deemed as the most accurate studies in informing researchers as to the aetiology of PMD and SAD. This is because studies which recruit cases from non-first episode samples, are effectively sampling cases in treatment. Cases with a chronic course of illness and poor outcomes are more likely to be in contact with services and this may lead to sampling from a more unwell population than from all psychosis incidence cases. This may lead to an inaccurate estimation of the effect of aetiological factors. Similarly, studies which only focus on inpatients are arguably sampling from a more ill population and therefore give a skewed picture of the aetiology of a disorder. Incidence studies provide a more representative view of all incident cases and therefore a more representative view of the course and outcome.

3.9. Summary

The above literature highlights several important points. Firstly, there are very few studies on psychosocial risk factors in psychosis which include PMD and SAD. Secondly, the psychosocial risk factors reviewed above are clearly important in the aetiology of psychosis in general and non-psychotic depression and therefore are likely to be important in PMD and SAD. Finally, studies which have been conducted have some very important limitations (see section 3.8). Therefore, this thesis aimed to examine the psychosocial risk factors mentioned above in PMD and SAD cases, but within a study that overcomes these three major methodological issues (separating PMD and SAD cases from other diagnoses, sampling from a first episode psychosis sample, accounting for diagnostic stability).

The literature review above indicated that interactions between various risk factors are potentially important. However, as there was very little research available on the risk factors for PMD and SAD, the aim of this thesis was to conduct preliminary analyses on the risks for these disorders on which future studies can build.

3.10. Hypotheses

The following hypotheses were based on the literature discussed above:

1. PMD and SAD would be associated with being of non-white British ethnicity, being female, being born outside the UK, being older and being in the London site.
2. Lower educational attainment would be more frequent in PMD and SAD cases compared with controls.
3. Factors associated with social isolation, such as living situation, relationship status and contact with friends, would be more frequent in PMD and SAD cases compared with controls.
4. Unemployment would be more frequent in PMD and SAD cases compared with controls.
5. Childhood adversity would be more frequent in PMD and SAD cases compared with controls.
6. Independent life events would be more frequent in PMD and SAD cases in the year prior to illness onset compared with controls.

Within this thesis, as well as examining the risk factors associated with PMD and SAD compared with controls, these factors were also examined in schizophrenia and bipolar disorder cases compared with controls. This was in order to examine effect sizes in the different diagnostic groups.

CHAPTER 4. A systematic review of the course of illness and outcome of PMD and SAD

"When a patient or family member asks how much time is needed to recover from an episode of psychotic depression, a clinician usually cannot give a precise answer."[161]

Rothschild (2009)

4.1. Aims of the chapter

The aims of this chapter were to describe and report a systematic review of the course of illness and outcome of PMD and SAD, and to detail hypotheses derived from the review.

4.2. Why it is important to do this review

Although there have been a number of literature reviews on the outcomes of PMD and SAD,[162-166] there have been no systematic reviews of the literature. Therefore, the aim of this chapter was to report findings from a systematic review of all literature reporting on any outcomes over any time periods for PMD and SAD.

4.3. Systematic review methodology

This review is reported in line with the recommendations from the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[167, 168]

4.3.1. Criteria for considering studies for this review

4.3.1.1. Types of studies

This review included all follow-up, longitudinal, retrospective and prospective studies with primary data (there was no minimum follow-up period). Literature reviews and systematic reviews were excluded but reference lists from reviews were checked for potentially relevant papers that had not been identified in the searches. RCTs and clinical trials were excluded. Papers of all languages were included.

4.3.1.2. Types of participants

Participants of both genders, aged 16+ years were included in the review. At least some of the participants in the study must have had a diagnosis of PMD or SAD (no minimum percentage was set, even if studies had one PMD or SAD participant they were included) based on any diagnostic system. Studies focussing on adolescents, those with diagnostic groups which included mixed diagnostic groups (e.g. PMD cases and schizophrenia cases analysed together in the same group) and studies in which the diagnosis was unclear were excluded. Papers focussing solely on older adults (all participants age over 60) were also excluded as this was not the focus of this thesis.

4.3.1.3. Types of outcome measures

The outcomes of interest were: mortality and suicidality (e.g. deaths, completed suicide, suicide attempts, self-harm); diagnostic stability; course of illness (e.g. recovery, remission, relapse (defined by the author of each paper)); all psychosocial outcomes (e.g. functioning as measured by the GAF, relationship status, employment status); and service use. Any other biological or medical outcomes were not included.

4.3.2. Search strategies for identification of studies

4.3.2.1. Electronic searches

The following electronic databases were searched: Ovid SP PsychInfo (1806 to April week 5 2010); Ovid SP EMBASE Classic and EMBASE (1947 to 2010 week 17); and OVID Medline (R) (1950 to April week 5 2010).

The following search strategy was used:

1. schizoaffective/

2. schizoaffective.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

3. delusional depress*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

4. psychotic depress*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

5. depressive psycho*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

6. psychotic major depress*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

7. major depression with psychotic features.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

8. 1 or 2 or 3 or 4 or 5 or 6 or 7

9. case control studies/

10. case control studies.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

11. case control.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

12. cohort studies/

13. cohort studies.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

14. cohort.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

15. follow-up studies/

16. follow-up studies.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

17. follow-up.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

18. retrospective studies/

19. retrospective studies.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

20. retrospective.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

21. prospective studies/

22. prospective studies.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

23. prospective.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

24. systematic review/

25. systematic review.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

26. literature review/

27. literature review.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

28. meta analysis/

29. meta analys*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

30. qualitative research/

31. qualitative.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

32. quantitative research/

33. quantitative.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

34. longitudinal studies/

35. longitudinal.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

36. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35

37. 8 and 36

38. limit 37 to human

39. 38 not experimental design.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

40. 39 not drug therapy.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

41. 40 not treatment effectiveness.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

42. 41 not trial.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

43. remove duplicates from 42

4.3.2.2. Searching other resources

Further potentially relevant material was searched for by checking reference lists of included papers and checking reference lists of reviews found in the search as well as reviews already known about.

4.3.3. Data Collection and Analysis

4.3.3.1. Selection of studies

The following steps were followed:

1. The search was completed as specified, all results were added into a reference manager and duplicates removed.
2. All titles and abstracts were examined to remove obviously irrelevant papers. If there was any uncertainty about whether the study met criteria based on title and abstract, the full paper was obtained.
3. The full text of all potentially relevant papers were retrieved.
4. The full text of papers were examined for consistency with study criteria.

5. Two independent reviewers discussed and resolved any differences in opinion about studies which were included/excluded.
6. Multiple reports of the same study were linked together.
7. Reference lists of included papers and reviews were checked to make sure no papers had been missed.

4.3.3.2. Data extraction and Management

Two investigators independently extracted data from the studies. Any disagreements in the data extraction were resolved by discussion. Forms were designed for the purpose of recording extracted data (see Appendix A). The following information was collected from each study:

Methods: Study design, duration of study / follow-up period, study setting, country. Within this review, the following definitions were used; prospective study - recruits participants and follows them forward in time; retrospective study – recruits participants and looks back at their history; historical study - selects participants from historical case notes, locates the participant and follows them forward in time.

Participants: Total number entered into study, diagnostic tool used, sample selection and recruitment, comparison group (if applicable).

Outcomes: Any outcome measures were acceptable.

Results: Total number of participants followed up / entered into the analyses, summary data for groups (mean and SD, median and range or frequencies and percentages for main outcome), subgroup analyses (including mood congruent versus mood incongruent psychotic symptoms).

4.3.3.3. Assessment of quality in included studies

The Newcastle-Ottawa Scale was used as a quality assessment (this version is no longer available online but the newer version can be viewed at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp for newer version). The scale was modified for the purpose of this review by removing a question deemed to be irrelevant ("Demonstration that outcome of interest was not present at start of study") and including 3 questions on multivariable analyses, appropriate analyses and confidence intervals (see Appendix B for the modified version of the scale). Some of the questions were considered to be subjective so criteria were set to ensure consistency (see Appendix B). Criteria on the representativeness of the exposed cohorts were decided upon by both of the reviewers. Criteria on adequacy of the follow-up of the cohorts were based on a paper by Kristman et al., which discusses what levels of attrition are acceptable.[169]

Although a quality assessment scale was used, during the course of the review it became apparent that a more critical indication of study quality was based on what participant selection was used (this is discussed further in section 4.4.2). Therefore, although Newcastle-Ottawa Scale scores were reported in the included studies information, throughout the results, participant selection is referred to in relation to quality.

4.4. Results

4.4.1. Description of studies

4.4.1.1. Results of the search

The PsychInfo search produced 788 results, EMBASE 1860 results and Medline 1101 results (see figure 4-1 for flow diagram). This gave a total of 3749 papers found from

searches. To this, 63 papers, which were identified from the reference lists of literature reviews and included papers, were added to give a total of 3812 papers. When duplicates were removed a total of 2737 remained. After reading all titles and abstracts, 2270 were removed leaving a total of 467 papers, of which 44 were in languages other than English. Efforts were made to retrieve all foreign language articles but unfortunately a small number (4) were unavailable from the British library (and via contacting the authors directly) and were therefore excluded. All available foreign language articles were either already in translated form or were translated by native or fluent speakers. After reading all 467 possibly relevant papers, 364 were excluded as they did not meet inclusion and exclusion criteria leaving a total of 103 papers from the systematic search.

4.4.1.2. Excluded studies

Reasons for papers excluded are given in Table 4-1.

Table 4-1: Reason for paper exclusion

Reason for exclusion	Number
Review article	39
No course / outcome data	52
No PMD/SAD group	155
PMD/SAD mixed with other groups for outcome	88
Discussion / editorial	8
Sample under 18 years old	2
Not available from British Library	4
Other	7
Focus on older adults	9

4.4.1.3. Included studies

Table 4-2 presents all papers included in this review.

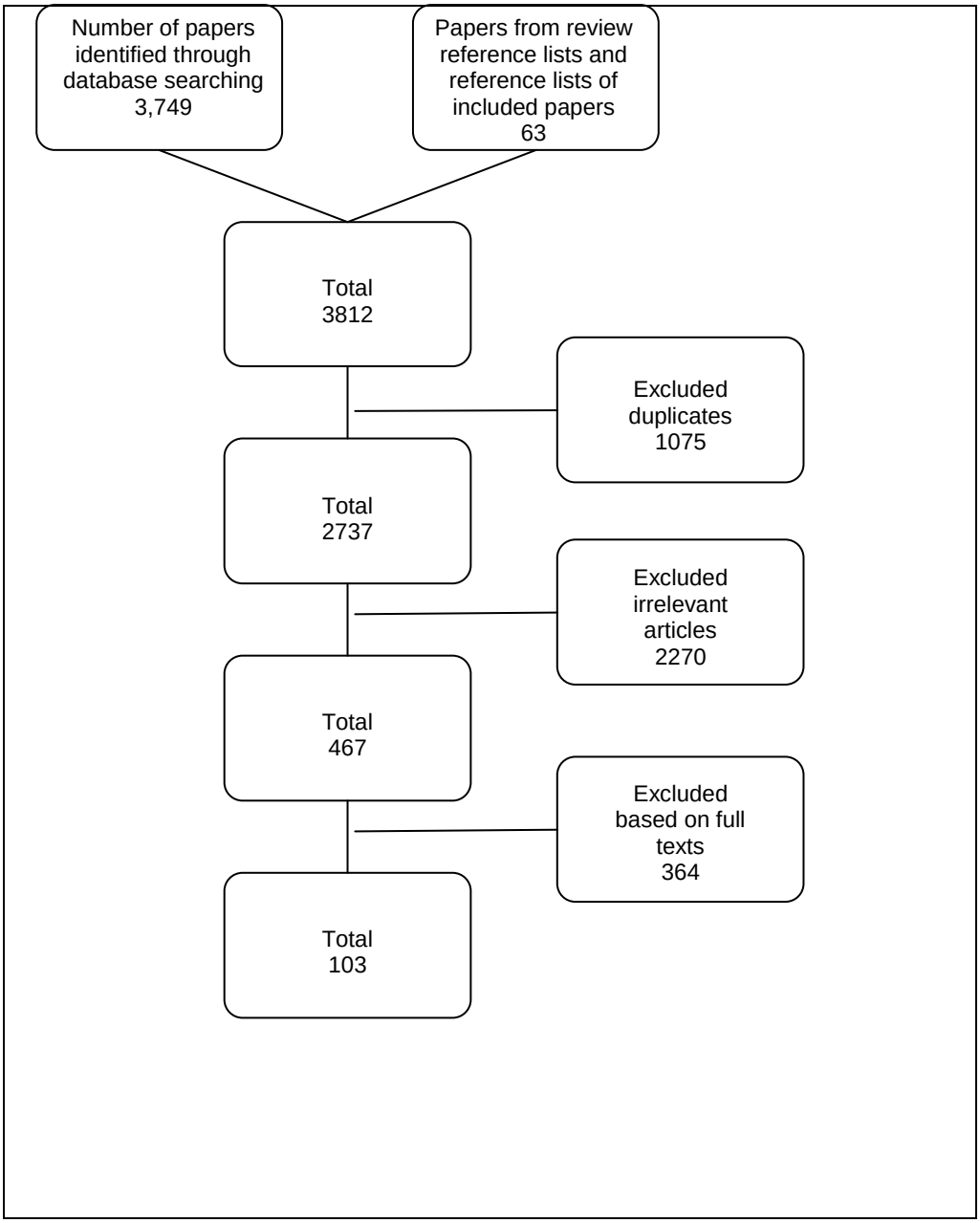


Figure 4-1: Consort diagram of paper exclusion

Table 4-2: Included papers

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
Amin[78] 1999	UK Nottingham	PMD	161 at follow-up (20 at follow-up)	95.8% (not reported)	Consecutive 1st contact inpatient and outpatients (1st episode)	ICD10 and DSM-III-R	Prospective 3 year follow-up	7
Baldwin[77] 2005	Ireland Cavan & Monaghan	PMD	188 at follow-up (39 at follow-up)	97% (100%)	All first episode inpatient and outpatient psychosis or manic cases referred to secondary services	DSM-IV	Prospective 6 month follow-up	9
Charney[170] 1981	USA New Haven	PMD	120 at follow-up (54 at follow-up)	Retrospective	Consecutively admitted depressed inpatients	Mostly RDC	retrospective case control	6
Ciccone[171] 1975	USA, New York	PMD	no comparison group (150 at follow-up)	100%	All inpatients given a discharge diagnosis of psychotic depressive reaction	DSM I	Prospective 9 year follow-up	7
Copeland[172] 1983	UK London	PMD	47 at follow-up (29 at follow-up)	94% for some outcomes but less for a lot of others (unclear)	Consecutive series of inpatients from various hospitals with a primary diagnosis of depression	Non standardised PMD: True delusion / hallucination, depression worse in the mornings, diminution of sexual interest, loss of appetite, 10lbs + weight loss, unvarying depression, blames self. Neurotic depression: Depression worse in evenings, hard to sleep, no/slight diminution of sexual interest, no/slight	Retrospective case control study and prospective 5 year follow-up	5

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
						loss of appetite, < 10lbs weight loss, many neurotic symptoms e.g. anxiety, mood fluctuates markedly, blames others.		
Crebbin[1] 2008	UK Northumberla-nd	PMD	178 at follow-up (105 at follow-up)	100% (100%)	Inpatients and outpatients who had contact with the consultant following first episode of psychosis	ICD 10	Retrospective case control study and prospective 1 year follow-up	10
Forrester[173] 2001	UK Edinburgh	PMD	204 at follow-up (not reported)	Retrospective	Inpatients discharged between 1993-1994 with psychosis and at least 2 admission	ICD-9	Retrospective case notes study	6
Frances[174] 1981	USA New York	PMD	64 at follow-up (30 at follow-up)	not reported	Inpatients with depression who had participated in a prior study	RDC	Prospective follow-up (length missing)	4
Frangos[72] 1983	Greece Athens	PMD	264 at follow-up (145 at follow-up)	Retrospective	Selected inpatients discharged with depression	RDC (psychotic depression = delusions, hallucinations or stupor)	Retrospective case control study	7
Glassman[175] 1981	USA New York	PMD	63 at follow-up (21 at follow-up)	Retrospective / 100%	consecutively admitted depressed inpatients	RDC – only mood congruent, paranoid delusions included only if mood congruent	Retrospective case control study and prospective 2 week follow-up	5
Helms[176] 1983	USA Iowa	PMD	No comparison (13 at follow-up)	no comparison (100%)	All inpatients with PMD with 2 or more admissions	RDC (hallucinations and delusions)	Historical case notes review	9

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
Hill[177] 2009	USA Illinois	PMD	67 at follow-up (9 at follow-up)	60% (43%)	Consecutive psychotic inpatients admitted with recent onset	DSM 4	Prospective 6 week follow-up	5
Hori[178] 1993	Japan Tsukuba	PMD	93 at follow-up (38 at follow-up)	100% Retrospective	Inpatients hospitalised for depression	DSM3R – delusions and hallucinations	Retrospective case control study	6
Isometsa[179] 1994	Finland Helsinki	PMD	70 at follow-up (24 at follow-up)	Retrospective	Random sample of all suicides with depression over 1 year period	DSM3R	Retrospective case control study	7
Jager[180] 2005	Germany Munich	PMD	117 at follow-up (20 at follow-up)	64% (not reported)	Consecutive first admission inpatients with functional psychosis	DSM4	Historical 15 year follow-up	7
Johnson[73] 1991	USA Multiple cities	PMD	624 at follow-up (92 at follow-up)	80.4% (80.7%)	General population sample with a lifetime diagnosis of PMD or non-psychotic major depression	DSM 3 - delusions and hallucinations only	Prospective 1 year follow-up	7
Kessing[181] 2003	Denmark -	PMD	3455 at follow-up (1275 at follow-up)	100% (100%)	First ever discharge from inpatient services with a depressive diagnosis	ICD-10	Prospective 1-6 year follow-up	10
Lenzi[182] 1996	Italy Pisa	PMD	144 at follow-up (11 at follow-up)	not reported	Consecutively admitted female inpatients admitted for manic, mixed, depressive or SA episode	DSM-IV	Prospective 3 year follow-up	4

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
Leyton[183] 1995	Canada Quebec	PMD	165 at follow-up (25 at follow-up)	Retrospective	Alphabetically consecutive former patients from inpatients and outpatients excluding SA ps.	DSM3R / RDC to exclude SA (congruent PMD only)	Retrospective case control study	8
Lykouras[184] 1994	Greece Athens	PMD	73 at follow-up (32 at follow-up)	75.3% (not reported)	Hospitalised inpatients with unipolar depression	DSM3 – mood congruent only	Prospective 6 year follow-up	4
Maj[185] 2007	Italy Naples	PMD	331at follow-up (66 at follow-up)	73.2% (76%)	Consecutive new inpatients and outpatients with depression	DSM3	Prospective 10 year follow-up and retrospective data	9
Parker[186] 1991	Australia, Sydney	PMD	70 at follow-up (35 at follow-up)	unclear	Consecutively diagnosed depressed inpatients and outpatients	DSM3 / RDC / ICD9 (PMD met DSM3 criteria for melancholia and psychosis, RDC criteria for endogenous depression and psychosis and evidence of delusions and/or hallucinations)	Prospective 12 month follow-up, further follow-up not clear	6
Pederson[187] 1972	USA New York	PMD	No comparison group (568 at follow-up)	100%	All inpatient and outpatients who received a diagnosis of PMD on their initial registration (not first episode)	Not reported	Retrospective case notes review and prospective 5 year follow-up	9
Radomsky[188] 1999	USA Pittsburgh	PMD	1,048 at follow-up	Retrospective	Consecutively admitted psychotic inpatients from	DSM3R	Retrospective case control	7

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
			(85 at follow-up)		1992 – 1994		study	
Robinson[189] 1985	USA New York	PMD	102 at follow-up (52 at follow-up)	98% (100%)	Inpatients admitted with depression	RDC - (those with only hallucinations or depressive stupor were excluded)	Historical 1 year follow-up from discharge	7
Roose[190] 1983	USA New York	PMD	39 at follow-up (6 definite, possibly 10 at follow-up)	Retrospective	Every patient who committed suicide from 1955-1980	RDC & DSM3	retrospective case notes review	7
Schimmelmann[191] 2005	Australia Melbourne	PMD	492 at follow-up (12 at follow-up)	74% (not reported)	Consecutively admitted inpatients to the early psychosis prevention and intervention centre	DSM-IV	Prospective 18 month follow-up	9
Stephens[192] 1982	USA Baltimore	PMD	283 at follow-up (10 at follow-up)	missing	First admission inpatients admitted for at least 21 days	RDC	Historical 5-16 year follow-up	4
Suominen[193] 2009	Finland Helsinki	PMD	1820 at follow-up (110 at follow-up)	100% (100%)	All inpatients hospitalisations with major depression and attempted suicide	ICD-10	Prospective 4.2 year follow-up	10
Videbech[194] 1995	Denmark	PMD	50 at follow-up (14 at follow-up)	100% (100%)	1st admission inpatient women with first episode of psychosis within 12 months of parturition	ICD-8	Prospective 11 year (7-14 years) follow-up	7
Vythilingham[195] 2003	USA Yale	PMD	120 at follow-up (61 at follow-up)	100% (100%)	Inpatients who had participated in a prior study	RDC / DSM3 / DSM3R – PMD defined by hallucinations and delusions	Prospective 15 year follow-up	6
Welner[196] 1977	USA Missouri	PMD	114 at follow-up (64 at follow-up)	89% (not reported)	First admission inpatients with schizoaffective and	Not reported	Prospective 7.6-8.9 year	4

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
					related psychoses		follow-up	
Whitty[197] 2005	Ireland Dublin	PMD	147 at follow-up (11 at follow-up)	89% follow-up rate, actually 86% (not reported)	1st episode psychosis cases presenting to inpatients and outpatient services	DSM4	Prospective 4 year follow-up	9
Wolfersdorf[198] 1987	Germany, Ravensburg	PMD	92 at follow-up (46 at follow-up)	Retrospective	Inpatients admitted to a depression ward	ICD unspecified	Retrospective case notes study	7
Maj[199] 1990 *Naples overlapping samples	Italy Naples	PMD	55 at follow-up (27 at follow-up)	76% (75%)	All inpatients and outpatients referred with major depressive disorder	DSM3	Prospective 6 month and 7 year follow-up	6
Williams[200] 1987 *Chestnut Lodge	USA Maryland	PMD	294 at follow-up (44 at follow-up)	81% (76%)	Severely ill inpatients in long-term residential centre	DSM3	Prospective 2-32 year follow-up	6
Angst[201] 1986 *Angst 86?	Switzerland Zurich	PMD	388 at follow-up (73 at follow-up)	96% (not reported)	Admitted inpatients with unipolar and bipolar affective disorders	DSM3	Prospective 17-21 year follow-up	4
Winokur[202] 1985 *Angst 86?	Switzerland Zurich	PMD	89 at follow-up (29 at follow-up)	Retrospective	Admitted inpatients with affective and schizoaffective disorders	ICD8	retro case control study	6
Aronson[203] 1987 *Aronson study	USA New York	PMD	52 at follow-up (42 at follow-up)	72% (not reported)	Delusional depression inpatients who received outpatient treatment for at least 6 months	DSM3	Historical 3.5 year (0.5-6 years) follow-up	5
Aronson[204] 1988a	USA New York	PMD	52 at follow-up (42 at follow-up)	unclear	Delusional depressive inpatients admitted and	DSM3	Historical 6 month follow-	5

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
*Aronson study					discharged in remission and follow-up for at least 6 months by outpatients		up	
Coryell[205] 1986a * Coryell 86	USA Iowa	PMD	65 at follow-up (65 at follow-up; 23 congruent, 42 incongruent)	not stated	Selected from inpatients consecutively admitted for depressive symptoms	DSM3	prospective 6 month follow-up	4
Coryell[206] 1986b *Coryell 86	USA Iowa	PMD	205 at follow-up (46 at follow-up)	87% (83.6%)	Consecutively admitted inpatients with depression	DSM3 (depression with no history of mania)	Prospective 6 month follow-up	5
Miller[207] 1987 *Miller papers	USA New York	PMD	90 at follow-up (45 at follow-up)	Retrospective	Consecutively discharged inpatients with depression	DSM3	Retrospective case control study	9
Miller[208] 1988 *Miller papers	USA New York	PMD	no comparison (45 at follow-up)	Retrospective	Consecutively discharged inpatients with PMD	DSM3	Retrospective case notes review	9
Black[209] 1988 *IOWA 70-81	USA Iowa	PMD	1593 at follow-up (183 at follow-up)	unclear possibly 100%	Inpatients with an affective disorder followed up on a death register	DSM3 excluding stupor	Prospective 0-14 year follow-up	7
Winokur[210] 1992 *IOWA 70-81	USA Iowa	PMD	unclear (unclear)	unclear	Admitted inpatients with an affective disorder	DSM3 and DSM-III-R for congruent and incongruent PMD	Prospective 2 year follow-up	4
Coryell[211] 1982a *IOWA 500	USA Iowa	PMD	variable 143-223 at follow-up	variable: discharge 99% (99%)	Consecutive inpatients with unipolar depression	Feigner criteria excluding stupor	Historical short term 3.4-5 year follow-up and	7

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
			(79-122 at follow-up)	short term 90% (86%) Death 99% (not reported) Diagnosis 64% (65%)			long-term 20 year follow-up	
Coryell[212] 1982b *IOWA 500	USA Iowa	PMD	various 2-3 years follow-up non-somatic therapies only 411 (congruent 71, incongruent 43) 2-3 years follow-up (congruent 95, incongruent 88) 5 years follow-up (congruent 26, incongruent 21)	unclear	All admissions with a primary discharge diagnosis of affective disorder or schizophrenia	DSM3 / RDC	Prospective 2-3 year follow-up	7
Coryell[213] 1985 *IOWA 500	USA Iowa	PMD	602 at follow-up (190 at follow-up)	94% (94%)	All inpatients with schizophrenia, manic depression or involutional melancholia	DSM3	Historical 40 year follow-up	7
Akiskal[214] 1995 *NIMH collaborative	USA various	PMD	No comparison (559 at follow-up)	not reported	Consecutive inpatients and new outpatients excluding those with a history or mania or	RDC	Prospective 2-11 year follow-up	8

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
depression study					hypomania			
Coryell[215] 1987a *NIMH collaborative depression study	USA various	PMD	506 at follow-up (55 at follow-up)	87.8% (not reported)	Inpatients and outpatients with non-bipolar depression	RDC modified – hallucinations and delusions; FTD, stupor and severe impairment were not sufficient for a PMD diagnosis	Prospective 6-24 months follow-up	7
Coryell[216] 1997 *NIMH collaborative depression study	USA Iowa	PMD	327 at follow-up (58 at follow-up)	69% (71%)	Sample of inpatients and outpatients seeking treatment in tertiary care centres with MDD, mania or SA.	RDC – broadened to approximate DSM-IV more closely – RDC SA subtypes included as PMD with the exception of mainly schizophrenia subtype. Therefore PMD here approximates DSM-IV PMD.	Prospective 5 year follow-up	6
Del Bello[217] 2003 *McLean	USA Massachusetts	PMD	no comparison (140 at follow-up)	no comparison (89%)	First admission inpatients with affective psychoses	DSMIV	Prospective 1-2 year follow-up	8
Tohen[218] 1992 *McLean study	USA Boston	PMD	102 at follow-up (15 at follow-up)	100% (100%)	First admission inpatients with psychosis	DSM3R	Prospective 6 month follow-up	8
Tohen[219] 2000a *McLean study	USA Massachusetts	PMD	181 at follow-up (45 at follow-up)	83% (75%)	First admission inpatients with PMD or BP	DSM4	Prospective 6-24 months follow-up	9
Tohen[220] 2000b *McLean study	USA Massachusetts	PMD	257 at follow-up (44 at follow-up)	85.5-86.8% (not reported)	First episode inpatients with psychosis	DSM-IV	Prospective 6 month follow-up	8

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
Goldberg[221] 2001 *Chicago follow-up study	USA Chicago	PMD	74 at follow-up (10 at follow-up)	~80% (not reported)	hospitalised depressed inpatients	RDC with no prior history of mania or hypomania	Prospective 15 year follow-up	6
Goldberg[222] 2004 *Chicago follow-up study	USA Chicago	PMD	123 at follow-up (17 at follow-up)	80% (not reported)	Inpatients hospitalised for bipolar I disorder, PMD or NPMD	RDC	Prospective 10 year follow-up	9
Goldberg[223] 2005 *Chicago follow-up study	USA Chicago	PMD	124 at follow-up at 7-8 years (17 at follow-up at 7-8 years)	79% at 7-8 years (63%)	Relatively early young inpatients	RDC	Prospective 7-8 year follow-up with 4.5 year and 2 year follow-ups	7
Kettering[224] 1987 *Chicago follow-up study	USA Chicago	PMD	110 at follow-up (31 at follow-up)	not reported	Admitted inpatients from 2 sites	RDC	Prospective 14 month follow-up (range 12-26 months)	5
Sands[225] 1994 *Chicago follow-up study	USA Chicago	PMD	94 at follow-up (31 at follow-up)	85% (not reported)	Inpatients admitted with depression	RDC	Prospective mean 2.4 year follow-up (1-5 years)	6
Sands[226] 1995 *Chicago follow-up study	USA Chicago	PMD	92 at follow-up (22 at follow-up)	85% (not reported)	Hospitalised inpatients with depression	RDC	Prospective 2 and 4.5 year follow-up	6
Bromet[227] 1996 *Suffolk county	USA New York	PMD	202 at follow-up (42 at follow-up)	90% (not reported)	1st admission (within 6 months) inpatients with psychosis	DSM3R	Prospective 6 month follow-up	8
Craig[228] 1997	USA New York	PMD	202 at follow-up (42 at follow-up)	90% (not reported)	first admission inpatients with psychosis	DSM3R	Prospective 6 month follow-	6

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
*Suffolk county							up	
Craig[229] 2000 *Suffolk county	USA New York	PMD	335 at follow-up (70 at follow-up)	89% unclear	First admission inpatients with psychosis	DSM3R / DSMIV	Prospective 2 year follow-up	7
Craig[230] 2006 *Suffolk county	USA New York	PMD	567 at follow-up (89 at follow-up)	90% (not reported)	First admission inpatients with psychosis	DSM3R	Prospective 10 year follow-up	7
Craig[231] 2007 *Suffolk county	USA New York	PMD	No comparison (87 at follow-up)	No comparison (94%)	First admission inpatients with psychosis	DSM3R	Prospective 2 year follow-up	10
Fennig[232] 1996 *Suffolk county	USA New York	PMD	150 at follow-up (27 at follow-up)	49% not reported	First admission inpatients with psychosis	DSM3R	Prospective 6 month follow-up	5
Naz[233] 2007 *Suffolk county	USA New York	PMD	No comparison (87 at follow-up)	No comparison (94%)	1st admission inpatients with psychosis	DSM4	Prospective 4 year follow-up	9
Schwartz[234] 2000 *Suffolk county	USA New York	PMD	547 at follow-up (103 at follow-up)	88% (not reported)	First admission inpatients with psychosis	DSM3R / DSM4	Prospective 2 year follow-up	9
Brockington[235] 1980	UK London	SAD	194 at follow-up (75 at follow-up)	not reported	Inpatients admitted between Dec 1972 – Dec 1974	CATEGO and RDC	Retrospective case control study and prospective 1-4 year follow-up	4
Coryell[236] 1988	USA Iowa	SAD	43 at follow-up (29 at follow-up)	not reported	Consecutively admitted inpatients with a functional psychosis excluding mania	RDC	Prospective 1 year follow-up	6
del Rio Vega[237]	Spain,	SAD	72 at follow-up	Retrospective	Inpatients from San	ICD 9 and RDC	Retrospective	6

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
1992	Madrid		(30 at follow-up)		Carlos University hospital 1981-1988		case control study	
Grossman[238] 1984	USA Chicago	SAD	120 at follow-up (24 at follow-up)	78-83% (not reported)	Inpatients admitted to one of two research hospitals	RDC & DSM-III	Prospective 13 month follow-up	4
Kendler[239] 1995	Ireland, Roscommon County	SAD	206 at follow-up (15 at follow-up)	unclear	All schizophrenia inpatients born after 1930 and a random sample of 75% of affective inpatients born after 1925.	DSM-III	Historical 60-65 year follow-up	8
Rice[240] 1992	USA	SAD	1213 at follow-up (7 at follow-up)	76% (not reported)	Admitted patients	RDC	Prospective 6 year follow-up	5
McGlashan[241] 1987 *Chestnut Lodge	USA Maryland	SAD	68 at follow-up (33 at follow-up)	78% (75%)	Severely ill inpatients at a long-term residential treatment place	DSM-III	Prospective 15 year follow-up	5
Maj[242] 1985 *Naples overlapping samples	Italy Naples	SAD	75 at follow-up (19 at follow-up)	80% (79%)	Inpatients and outpatients with affective disorders referred for treatment	RDC	Retrospective case control study and prospective 3 year follow-up	5
Angst[243] 1995a *Angst Zurich study	Switzerland Zurich	SAD	406 at follow-up (49 at follow-up)	100% (100%)	All inpatients with affective and schizoaffective patients admitted to clinic between 1959 – 1963	ICD9 (Unipolar depression defined as depression only, any occurrence of hypomania was classified as bipolar. SA disorder was diagnosed when evidence of mood-incongruent delusions and/or hallucinations).	Retrospective case control study and prospective 27 year follow-up	7

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
Angst[244] 1995b *Angst Zurich study	Switzerland Zurich	SAD	406 at follow-up (49 at follow-up)	100% (100%)	All inpatients with affective and schizoaffective patients admitted to clinic between 1959 – 1963	ICD-9	Prospective 27 year follow-up	7
Preisig[245] 1991 *Angst Zurich study	Switzerland Zurich	SAD	406 at follow-up (42 at follow-up)	100% (100%)	All inpatients with affective and schizoaffective patients admitted to clinic between 1959 – 1963	not reported	Prospective 22-26 year follow-up	8
Marneros[246] 1988a *Cologne study	Germany Cologne	SAD	72 at follow-up (37 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 (10-59) year follow-up	5
Marneros[247] 1988b *Cologne study	Germany Cologne	SAD	72 at follow-up (37 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 (10-59) year follow-up	5
Marneros[248] 1988c *Cologne study	Germany Cologne	SAD	72 at follow-up (37 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 (10-59) year follow-up	5
Marneros[249] 1988d *Cologne study	Germany Cologne	SAD	N/A (only SAD data useable) (36 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 year follow-up	5
Marneros[250] 1989a *Cologne study	Germany Cologne	SAD	72 at follow-up (37 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 year follow-up	5
Marneros[251] 1989b *Cologne study	Germany Cologne	SAD	72 at follow-up (37 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 year follow-up	5
Marneros[252] 1989c	Germany Cologne	SAD	72 at follow-up (37 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 year	5

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
*Cologne study							follow-up	
Marneros[253] 1990a *Cologne study	Germany Cologne	SAD	207 at follow-up (45 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 year follow-up	5
Marneros[254] 1990b *Cologne study	Germany Cologne	SAD	207 at follow-up (45 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 year follow-up	5
Marneros[255] 1991 *Cologne study	Germany Cologne	SAD	355 at follow-up (48 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.2 year follow-up	2
Rohde[256] 1990 *Cologne study	Germany Cologne	SAD	72 at follow-up (37 at follow-up)	not reported	Inpatients admitted between 1950-1979	DSM III modified	Prospective 25.6 year follow-up	5
Lenz[257] 1991	Austria Vienna	PMD & SAD	160 at follow-up (PMD: 38 at follow-up SAD: 11 at follow-up)	93% (not reported)	First admission inpatients with an ICD-9 diagnosis of 295, 296, 297 or 298	RDC	Prospective 7 year follow-up	6
Opjordsmoen[258] 1989	Norway Oslo	PMD & SAD	177 at follow-up (PMD: 50 at follow-up SAD: 33 at follow-up)	75% (PMD: 94% SAD: 45%)	First admission delusional inpatients from 1946-1948 and 1966-1967	DSM-III	Prospective 3-39 year follow-up	5
Tsuang[259] 1993	Iowa USA	PMD & SAD	65 at follow-up (17 Mood congruent PMD at follow-up 15 Mood incongruent PMD 11 SAD at	77% (not reported)	Inpatients discharged between 1979-1982.	DSM-III	Historical 8 year follow-up	7

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
			follow-up)					
Coryell[260] 1987b *DST 6mo study	Iowa USA	PMD & SAD	95 at follow-up (PMD: 29 SAD: 46)	98% (PMD: 100% SAD: 98%)	Consecutively admitted inpatients with delusions and hallucinations were invited to participate. Mania excluded	RDC Also Feighner and DSM-III	Prospective 6 month follow-up	4
Galloway[261] 1995 *Chicago follow-up study	USA Chicago	PMD & SAD	122 at follow-up (PMD: 14 at follow-up SAD: 17 at follow-up)	not reported	Hospitalised inpatients aged 18-30	RDC	Prospective 4.5 and 6.7 year follow-up	5
Sands[262] 1999 *Chicago follow-up study	USA Chicago	PMD & SAD	187 at follow-up (PMD: 17 at follow-up SAD: 31 at follow-up)	not reported	Consecutively admitted inpatients between 18-35	RDC 3rd edition	Prospective 7.5 year follow-up	6
Brockington[263] 1982	London UK	PMD/SAD mixed	site 1: 125 at follow-up site 2: 75 at follow-up (various)	site 1: 93% site 2: 69%	site 1: Consecutively admitted patients from 1966-1968 with a diagnosis of schizophrenia, paranoid psychosis, mania and PMD site 2: schizoaffective inpatients sampled from 1972 - 1975	ICD-8 (Catego; RDC; DSM) PMD and SAD overall in these categories	Prospective 1-6.5 year follow-up	5
Van Praag[264] 1984	Utrecht Netherlands	PMD/SAD mixed	133 at follow-up (12 SA melancholia at follow-up	Not reported	Inpatients with functional psychoses with a subsequent follow-up over several years	Own criteria: Melancholic schizoaffective – depressed mood, psychomotor agitation or inhibition plus	Prospective 4-7 year follow-up	4

Reference	Country	Diagn-ostic group	Total sample size (PMD/SAD sample size)	Total follow-up rate (target group)	Selection process	Diagnostic tools	Study type	Quality assessment score
			12 SA depressive at follow-up)			mood congruent delusions / hallucinations Depressive schizoaffective: same as melancholic but with incongruent delusions / hallucinations. Affective and schizophrenia can be simultaneous or alternating.		
Coryell[265] 1995 *NIMH collaborative depression study	USA various	PMD/SAD mixed	600 at follow-up (not reported)	64% (not reported)	Sample of inpatients and outpatients seeking treatment in tertiary care centres with MDD, mania or SA.	RDC	Prospective 10 year follow-up	7
Coryell[266] 2008 *DST 6 month study	USA Iowa	PMD/SAD mixed	no comparison (28 PMD 26 SAD)	no comparison 100%	Consecutive inpatient admissions between 1982 and 1984	RDC	Prospective 17 year follow-up	9
Winokur[267] 1996 *DST 6 month study	USA Iowa	PMD/SAD mixed	69 at follow-up (22 PMD/SAD at follow-up 29 schizophrenia at follow-up 18 mixed at follow-up)	71% (not reported)	Consecutively admitted inpatients with non-organic and non-manic psychosis, split into those consistently diagnosed as schizophrenia or schizoaffective mainly schizophrenic in type versus PMD or schizoaffective mainly affective versus those who did not have a consistent diagnosis	RDC	Prospective 6 year follow-up	6

4.4.2. Findings

One hundred and three papers (from 60 studies) reported on the course and outcome of PMD and SAD. The related papers are included within this review but are highlighted throughout to prevent double counting of the same data. Seventy papers reported on the outcomes for patient groups with PMD, 22 reported on the outcomes for patient groups with SAD, 6 reported on the outcomes for PMD and SAD groups separately and 5 reported on the outcomes for these groups combined.

The papers were based on data collected in numerous countries spanning 4 continents: Asia; Australia; Europe; and North America. The majority (101) were from Europe and North America (42 and 59 papers consecutively). The articles included 71 papers from prospective studies, 13 papers from retrospective studies, 9 papers from historical studies and 10 papers which came from studies which used multiple methods (9 papers which report on data from retrospective and prospective data and 1 which reports on data from historical and prospective sources). The prospective studies ranged from 6 weeks to 39 years. The historical studies ranged from 6 months to 65 years follow-up. The participant selection from all the studies can loosely be grouped into six categories: first episode inpatients and outpatients (incidence samples; n4); first admission patients (n18); inpatients only (not first episode; n67); non-first episode inpatients and outpatients (n10); first episode inpatients (n1); and other (n3). As discussed in section 3.8, incidence samples minimise biasing results toward more ill patients and therefore poor outcomes and, within this review, studies based on these samples are therefore judged to be superior in quality.

The included papers used a variety of diagnostic classification systems including feigner criteria, RDC, and a number of DSM and ICD iterations. As discussed in chapter 2,

definitions of PMD and SAD have changed over time and different diagnostic classifications do not always match exactly making comparisons between studies difficult. This is especially the case in the studies that used non-standardised definitions,[172, 264] others which used modified criteria[175, 189, 209, 216, 268-270] and several which do not state what diagnostic classification they used.[245, 271, 272] However, the majority of the studies used either the RDC or DSM-3 or later versions of the DSM, all of which are the most consistent criteria for what is defined as PMD and SAD currently.

In terms of diagnostic comparison groups, of the 103 papers, 13 had no comparison groups, 38 compared the target group to other affective groups, 30 compared the target group to other psychotic disorders, and 22 compared the target group to a combination of psychotic and affective diagnostic groups. Within this thesis, PMD and SAD cases compared with the other major psychotic diagnostic groups of schizophrenia and bipolar cases are the main interest so will be focussed on in this review, although results are displayed for all diagnostic groups.

Due to the methodological, clinical and statistical heterogeneity of the studies and data, it was not valid to conduct meta-analyses on the data so the findings are reported as a narrative review. Due to the large number of papers identified and the range of outcome measures examined, the results of the review were divided into 6 sections: diagnostic stability; course of illness; mortality and suicidality; psychosocial outcomes; and service use.

4.4.2.1. Diagnostic stability

Of the 103 papers identified for this review, 28 had data on diagnostic change or stability. The studies on diagnostic change can be split into those on prospective

consistency and those on retrospective consistency. Prospective consistency is defined as the proportion of cases who have the same diagnosis at follow-up as they did at baseline. Retrospective consistently is defined as the proportion of cases who have the same diagnosis at baseline as they do at follow-up.

4.4.2.1.1. Prospective consistency

Of the 28 papers which reported on prospective consistency, 24 had useable data. Table 4-3 shows the prospective consistency for each diagnostic group. When all studies are included the prospective consistencies range from 24-100% for PMD, 18-83% for SAD, 30-97% for psychotic bipolar disorder and 50-100% for schizophrenia. This wide variation in prospective consistency is likely due to the large amount of heterogeneity of the studies included in the review (i.e. different diagnostic tools, widely varying follow-up lengths, differing samples and differing quality).

If only long-term studies are included (defined here as 8+ years), then the range of prospective consistencies reduces dramatically for schizophrenia but not for the other disorders: 20-93% for PMD; 58-84% for SAD; 33-75% for psychotic bipolar disorder; and 90-100% for schizophrenia cases. If the most recent versions of the DSM and ICD are used (or second most recent for DSM as there are no studies examining the most recent version of the DSM), then the prospective consistencies get much narrower especially for PMD and psychotic bipolar disorder indicating that more current classification systems may be more valid for these disorders: 65-100% for PMD; 64-97% for psychotic bipolar disorder; and 58-97% for schizophrenia. There were no studies on SAD which used ICD-10 or DSM-IV.

If only studies based on an incidence samples are included,[1, 77, 78, 197] the prospective consistencies are 65-95% for PMD, compared with 78-97% for psychotic bipolar disorder and 82-96% for schizophrenia. No incidence sample studies examined SAD cases. These estimates are a lot narrower and more similar to each other but the longest of these is only four years, thus the long term prospective consistency is unknown.

Based on incidence studies, PMD cases have a wider range of prospective consistencies which include lower boundaries compared with schizophrenia and bipolar cases. Therefore, it was hypothesized that PMD would have lower prospective consistency compared with schizophrenia and bipolar cases. Data on SAD cases was not available from incidence studies. However, due to the similarities between PMD and SAD cases in terms of symptoms (see Chapter 2) and the fact that the range of prospective consistencies are similar between PMD and SAD in the comparisons based on all studies and based on 8+ years studies, it was also hypothesized that SAD would have lower prospective consistency compared with schizophrenia and bipolar cases.

Table 4-3: Prospective consistency (expressed as a percentage)

Reference	Diagnostic instrument	Time frame	PMD	SAD	NPMD	NPBP	PBP	SZ	Other psychoses	Other
Amin[78]	DSM-III	3 years	70	-	-	-	78	83	0-100	-
1999	ICD-10		65	-	-	-	91	82	20-69	-
Forrester[273]	Clinical diagnosis	retro	23.5	-	-	-	30	96.4	0	-
2001	RDC		50	-	-	-	83.3	65.5	5.3	-
	DSM-III-R:		-	-	-	-	63.6	75	30	-
	St Louis diagnosis		-	-	-	-	-	85.7	-	88.4
	ICD-10		-	-	-	-	63.6	57.6	-	22.2
Del Bello[217]	DSM-IV	1-2 years	87	-	-	-	-	-	-	-
2003										
*McLean										
Ciccone[274]	DSM I	9 years	81	-	-	-	-	-	-	-
1975										
Baldwin[77]	DSM-IV	6 months	95	-	-	-	97	-	50-100	-
2005										
Crebbin[1]	ICD-10	1 year	87	-	-	-	-	92	-	-
2008										
Jager[180]	DSM-IV	15 years	80	-	91	-	-	-	-	-
2005										
Johnson[73]	DSM-III	1 year	86.6	-	95.4	-	-	-	-	-
1991										
Kessing[181]	ICD-10	1-6 years	50.7	-	69-82.6	-	-	-	-	-
2003										
Maj[185]	DSM-III	10 years	89.9	-	95	-	-	-	-	96.8
2007										
Parker[275]	DSM3 / RDC / ICD9	1 year	89	-	86	-	-	-	-	-
1991										
Schimmelmann[191]	DSM-IV	1.5 years	100	-	-	-	83.2	97.3	40-94.1	-
2005										
Videbech[194]	ICD-8	11 years	64	-	-	-	33-75	100	40-73	67
1995										
Whitty[197]	DSM-IV	4 years	73	-	-	-	80	96	0-42	-
2005										
Coryell[276]	Feigner criteria (excluding stupor)	20 years	87	-	88	-	-	-	-	-

Reference	Diagnostic instrument	Time frame	PMD	SAD	NPMD	NPBP	PBP	SZ	Other psychoses	Other
1982a *IOWA 500										
Goldberg[221] 2001 *Chicago Follow-up Study	RDC with no prior history of mania or hypomania	15 years	20	-	66	-	-	-	-	-
Schwartz[234] 2000 *Suffolk county	DSM3R / DSM4	2 years	73.8	-	-	-	83	91.7	36.4-54.6	-
Copeland[172] 1983	Non standardised: *PMD: True delusion / hallucination, depression worse in the mornings, diminuation of sexual interest, loss of appetite, 10lbs + weight loss, unvarying depression, blames self.*	5 years	84	-	100	-	-	-	-	-
Lenz[257] 1991	RDC	7 years	79	27	-	-	47	81	78	-
Opjordsmoen[258] 1989	DSM-III	3-39 years	72	70	-	-	-	95	-	-
Marneros[255] 1991 *Cologne study	DSM III modified	25.6 years	-	58	79	0-14	-	90	23-50	-
Rice[240] 1992	RDC	6 years	-	43	74	33-53	-	50	60	16-80
Angst[277] 1995a *Angst & Preisig 1995 papers	ICD-9	27 years	-	83.8	65.5	78.9	-	-	100	-
Brockington[278] 1982	RDC	1-6.5 years	93%	18%	-	-	-	-	-	-

NPMD = non-psychotic major depression; NPBP = non-psychotic bipolar disorder; PBP = psychotic bipolar disorder; SZ = schizophrenia.

4.4.2.1.2. Retrospective consistency

Only three papers examined retrospective consistency (see Table 4-4). These papers reported a retrospective consistency of 82-100% for PMD, 76-89% for psychotic bipolar disorder and 50-73% for schizophrenia (no papers included data on SAD cases). Only one of the studies was based on an incidence sample and this indicated high retrospective consistency for PMD (100%) compared with schizophrenia and psychotic bipolar disorder (71% and 76% respectively). However, none of these papers were based on long-term studies highlighting the need for long-term studies on retrospective consistency in PMD and SAD cases.

Based on the literature above, it appears that in contrast to the findings on prospective consistency, retrospective consistency is higher in PMD cases compared with schizophrenia and bipolar cases. Therefore it was hypothesized that PMD would have higher retrospective consistency compared with schizophrenia and bipolar cases, and due to the similarities between PMD and SAD, it was hypothesized that SAD would have higher retrospective consistency compared with schizophrenia and bipolar cases too.

Table 4-4: Retrospective consistency (expressed as a percentage)

Reference	Diagnostic tool	Time period	PMD	PBP	SZ	SA general	Szform	Drug induced	Delusional disorder	Other psychoses
Whitty[197] 2005	DSM-IV	4 years	100	76	71	-	100	100	83	-
Schwartz[234] 2000 *Suffolk county	DSM3R / DSM4	2 years	81.7	84.8	73.1	44.4	85.7	-	-	72
Schimmelmann[191] 2005	DSM-IV	1.5 years	100	89.2	50.2	57.1	95	83.3	86.7	100

PBP = psychotic bipolar disorder; SZ = schizophrenia; SA general = schizoaffective disorder (general); Szform = schizophreniform.

4.4.2.2. Course of illness

Papers on course of illness included a large number of very heterogeneous outcomes including recovery, remission, recurrence, relapse, average number of episodes, average time in episode, time to recovery / remission, mean relapses and cycles. This makes grouping together similar outcomes very difficult. Therefore, this review has focussed on a few key course of illness markers: course type (episodic versus continuous); length and number of episodes; remission lengths; and amount of time psychotic.

Of the 103 papers identified for this review, 62 had data on course of illness in PMD and SAD (see Table 4-5). In terms of course of illness in relation to schizophrenia, three papers reported on course type in PMD and schizophrenia cases. All three papers reported PMD cases to have a less continuous illness (0% versus 10%;[258] 5% versus 41%;[200] 13% versus 34%[229]), and one reported PMD to have a more episodic course of illness (92% versus 16%), compared with schizophrenia cases. Opjordsmoen[258] also reported SAD cases to have a more episodic (82% versus 16%) and less continuous (0% versus10%) course type compared with schizophrenia cases. All three of these papers are based on inpatient only samples, although two are based on first admission inpatient samples,[229, 258] and two out of three of them are based on very long follow-ups (2-32 years[200] and 3-39 years[258]). Although none of these studies were compared statistically, they do indicate a trend. Based on this, it was hypothesized that PMD and SAD groups would have a higher proportion of cases with an episodic course of illness and less with a continuous course of illness compared with schizophrenia cases.

In relation to other key course of illness outcomes, only two papers reported on episode frequency or length. Opjordsmoen[258] reported that PMD and SAD cases had more episodes (mean 3.1 and 3.3 respectively versus 1.6) but shorter episodes (mean longest

episode 1.6 years and 4 years versus 26 years) compared with schizophrenia cases. Conversely, Tohen et al.[218] reported that PMD cases had longer episodes (days to recovery; mean 69 days (35.8 SD) versus 60 days (35.7 SD)). However, this study was only a 6-month follow-up study compared with the Opjordsmoen[258] paper which was based on a 3-39 year follow-upand neither paper compared the groups statistically. Although the literature on episode frequency and length is very limited, it was hypothesized that PMD and SAD would have: more episodes and shorter episodes compared with schizophrenia cases.

Of the 12 papers that included both PMD and schizophrenia course of illness information, nine reported on recovery or remission, with consistent findings: eight out of the nine reporting that PMD groups had more cases remitting/recovering compared with schizophrenia cases[200, 227, 229, 259, 279-282] (only one reported PMD to have shorter recovery times compared with schizophrenia cases[218]). All of these papers were based on data from inpatient samples (first admission and non-first admission). Although only 2 of these were statistically compared (and showed PMD to have statistically significantly better recovery), the studies indicate a trend. Based on this, it was hypothesized that PMD would have longer remissions and spend a smaller percentage of the follow-up psychotic compared with schizophrenia cases. Only two papers reported on recovery in SAD and schizophrenia cases and while one reported the same percentage recovered in each group,[259] the other reported higher recovery in the SAD group[283] (neither compared statistically). However, although both based on inpatient only samples, the second study was based only a six month follow-up[284] where as the first one was based on an 8 year historical study.[259] Based on these inconsistent and limited results, and the similarity between PMD and SAD cases in terms of symptoms plus the hypothesis based on PMD cases, it was hypothesized that SAD cases would

have longer remissions and spend a smaller percentage of the follow-up psychotic compared with schizophrenia cases.

There were also a number of studies which compared PMD and SAD groups to bipolar cases. Fifteen papers reported on course of illness in PMD and bipolar cases. The five papers which reported on course type had conflicting results. In terms of continuous course type, one study reported more PMD cases had a continuous course type compared with bipolar cases (24% congruent PMD and 21% incongruent PMD versus 5% congruent bipolar and 20% incongruent bipolar),[285] while another reported the opposite (5% PMD continuous versus 32% bipolar).[200] Both of these studies were long-term studies follow-ups based on inpatient samples. In terms of episodic course type, one paper reported PMD cases to be more episodic (9% PMD versus 5% bipolar),[286] while another two (both based on the same dataset) reported bipolar cases to be more episodic (83% PMD versus 100% bipolar).[203, 287]

In relation to bipolar comparisons on episodes, Angst et al.[288] includes details on number of episodes and reports PMD cases to have less episodes compared with bipolar cases (median 4 in congruent PMD and 5 in incongruent PMD versus 8.5 in congruent bipolar and 5 in incongruent bipolar) although this was not statistically tested (Winokur[289] also reports this but is based on the same dataset). Angst[290] also includes details on length of episodes and reports PMD cases to have longer episodes (median 5 months in congruent and incongruent PMD versus 4 months in congruent and incongruent bipolar). This trend is also reported by Lenzi et al.[182] who report a mean episode of 2.4 months in recurrent PMD cases and 4.7 months in single episode PMD cases compared with 1.1 and 2.5 months in psychotic bipolar I disorder and psychotic bipolar II disorder cases respectively. Again, neither of these comparisons are tested

statistically. The literature on number and length of episodes in PMD and bipolar cases is very sparse.

Angst et al.[291] also include several other relevant course of outcome variables. They report that time in episode was 28% and 21% for congruent and incongruent PMD cases respectively compared with 15% and 20% for congruent and incongruent bipolar cases respectively. They also report that time in remission was 40% and 19% for congruent and incongruent PMD cases respectively compared with 45% and 20% for congruent and incongruent bipolar cases respectively.[292] Neither of these outcomes have the statistical comparison tested between the groups. There are no other papers that report on these outcomes in PMD and bipolar cases.

Two studies report on number of episodes in SAD cases compared with bipolar cases. Maj[242] reported SAD cases to have a mean of 1.3 episodes (1.1 S.D.) prospectively compared with 0.8 episodes (1.4 S.D.) in the non-psychotic mania group. Angst et al.[293] reported a median of 6 episodes in the SAD group compared with 10 in the non-psychotic bipolar group. Angst et al.[294] also reported a median length of episodes of 3 months in SAD compared with 4.3 months in the non-psychotic bipolar group, and an average of 15% of time spent in illness in SAD cases compared with 19% in the non-psychotic bipolar group. There are no other papers that report on these outcomes in SAD and bipolar cases, or any papers which report on course type or length of remissions in SAD and bipolar cases.

The literature on course of illness in PMD and SAD cases compared with bipolar cases is sparse and conflicting. The inconsistency is likely due to the methodological differences between the studies included. These differences are also applicable to the

studies which compare PMD and schizophrenia cases. These include time period, sample and diagnostic system, but also, vitally, different ways of defining and measuring course of illness. As mentioned previously, incidence studies are of particular importance but there are no incidence studies examining course of illness. Due to the inconsistency of the findings comparing PMD and SAD with bipolar disorder, no hypotheses are stated.

Table 4-5: Course of illness

Reference	Findings	Comparisons
Ciccone[295] 1975	PMD: 95% were discharged home after hospital 76/150 had no subsequent psychiatric care 45/150 had 1 more occurrence of PMD. 29/150 had further episodes with a diagnosis other than PMD:	No comparison group.
Helms[176] 1983	12/13 had previous/subsequent psychotic depressive episodes. Previous: 1/13 had a purely psychotic previous admission. 1/13 had a mixed (psychotic and depressed) previous episode. 11/13 had a subsequent psychotic episode. 3/13 had a non-psychotic previous episode. Subsequent: 11/13 had a subsequent psychotic episode. 1/13 had a mixed subsequent episode.	No comparison group.
Pederson[296] 1972	PMD: 6% had only the baseline contact with services, 50% had a clear episode, received treatment and never had contact again, 24% had more than 1 episode, 20% had further episode that were not PMD .	No comparison group.
Del Bello[217] 2003 *McLean	PMD: 118/157 had syndromal recovery from index episode.	No comparison group.
Craig[231] 2007 *Suffolk county	PMD: 46.9% were experiencing 1st episode of depression 58.5% had at least 1 period of full remission lasting at least 2 months, 40% had a remission lasting at least 19/24 month follow-up. Of the participants who did not get a full remission, 41.2% were continually ill, 58.8% had a partial remission.	No comparison group.
Naz[233] 2007 *Suffolk county	PMD: 60/87 achieved a period of complete remission by 4 years, 20/87 had a partial remission, 7/87 did not remit at all. Median time to complete remission was 22.2 weeks. Cumulatively, 11.7% of remitters achieved this by 1 month, 36.7% by 3 months, 55% by 6 months, 71.7% by 1 year. 43.3% of remitters relapsed. 7 more experienced a partial relapse. Median time to relapse=60 weeks.	No comparison group.
Maj[185] 2007	PMD: 72/89 (81%) had at least one further episode of depression. NPMD: not reported. Depression with preoccupations: 88/123 (72%) had at least one further episode of depression.	Diagnostic groups not compared
Preisig[245] 1991 *Angst & Preisig 1995 papers	SAD: 1 episode = n1, 2 = n1, 3 = n7, 4 = n6, 5 = n3, 6 = n3, 7 = n5, 8 = n4, 9 = n0, 10 = n2, 11-15 = n10, 16-20 = n0, 20+ = n0. SAM: 1 episode = n0, 2 = n1, 3 = n2, 4 = n3, 5 = n8, 6 = n6, 7 = n11, 8 = n10, 9 = n3, 10 = n7, 11-15 = n20, 16-20 = n20, 20+ = n18. NPMD: 1 episode = n20, 2 = n31, 3 = n17, 4 = n18, 5 = n13, 6 = n10, 7 = n10, 8 = n4, 9 = n2, 10 = n4, 11-15 = n8, 16-20 = n5, 20+ = n2. NPBP: 1 episode = n0, 2 = n3, 3 = n6, 4 = n6, 5 = n7, 6 = n8, 7 =	Diagnostic groups not compared

Reference	Findings	Comparisons
	n10, 8 = n2, 9 = n10, 10 = n8, 11-15 = n19, 16-20 = n13, 20+ = n19.	
Opjordsmoen[258] 1989	SAD: Mean episodes 3.3 (1-14, NO SD), More than 1 episode 18/33 (55%), Mean longest episode 4 years, mean cycle duration 5 years (1-14, NO SD), 27/33 had an acute course of illness, 0/33 steadily psychotic, healthy by follow-up 14/33 (42%). PMD: Mean episodes 3.1 (1-16), More than 1 episode 23/50 (46%), Mean longest episode 1.6 years, mean cycle duration 9 years (1.3-36), 46/50 had an acute course of illness, 0/50 steadily psychotic, healthy by follow-up 33/50 (66%). SZ: Mean episodes 1.6 (1-10), More than 1 episode 8/94 (9%), Mean longest episode 26 years, mean cycle duration missing, 15/94 had an acute course of illness, 9/94 steadily psychotic, healthy by follow-up 9/94 (10%). Acute = without substantial residual symptoms between episodes. Mean duration of cycle = time from 1st symptoms in 1st episode to 1st symptoms in next episode. No details on scale etc. of psychosocial outcomes.	Diagnostic groups not compared
del Rio Vega[237] 1992	SAD: 0.78 (0.56SD) mean relapses. SABP: 0.78 (0.48SD) mean relapses.	Diagnostic groups not compared
Craig[229] 2000 *Suffolk county	PMD: 45/70 had complete remission, 16/70 had partial remission, 9/70 continuously ill. Sz/SA: 21/149 had complete remission, 77/149 had partial remission, 51/149 continuously ill. PBP: 93/116 had complete remission, 18/116 had partial remission, 5/116 continuously ill.	Diagnostic groups not compared
Coryell[297] 1986a * Coryell 86	55% of congruent group recovered. 33.3% of incongruent group recovered. No definition of recovery	Diagnostic groups not compared
Tohen[218] 1992 *McLean study	PMD: Days to recovery mean 69 (35.8 SD), days to recurrence mean 50 (64.3 SD), 11/14 had syndromal recovery, 3/13 had functional recovery, 1/10 had a relapse at 6 months, 7/15 had recovery at discharge. BP: Days to recovery mean 43 (31.9 SD), days to recurrence mean 99 (56.7 SD), 45/53 had syndromal recovery, 34/50 had functional recovery, 8/42 had a relapse at 6 months, 31/60 had recovery at discharge. SZ: Days to recovery mean 60 (35.7 SD), days to recurrence mean 56 (26.1 SD), 4/6 had syndromal recovery, 2/3 had functional recovery, 2/3 had a relapse at 6 months, 2/10 had recovery at discharge. Delusional disorder: Days to recovery mean 41 (17.8 SD), days to recurrence mean 43 (40.3 SD), 6/8 had syndromal recovery, 2/7 had functional recovery, 1/6 had a relapse at 6 months, 4/9 had recovery at discharge. Psychosis NOS / brief reactive psychosis: Days to recovery mean 50 (64.7 SD), days to recurrence mean 40 (- SD), 5/7 had syndromal recovery, 2/4 had functional recovery, 1/4 had a relapse at 6 months, 1/4 had recovery at discharge.	Diagnostic groups not compared
Tohen[298] 2000a *McLean study	PMD: 50/53 had a syndromal recovery, 13/45 had a functional recovery. PBP: 144/146 had a syndromal recovery, 55/136 had a functional recovery.	Diagnostic groups not compared

Reference	Findings	Comparisons
	Syndromal recovery was defined as no longer meeting criteria for an on-going DSM-IV illness episode. Functional recovery (yes/no), defined by comparing ratings on the Modified Vocational Status	
Tohen[299] 2000b *McLean study	PMD: syndromal recovery 75.0%, functional recovery 31.8%. 39.0 (11.5 SE) mean days to 25% recovery. BP manic: syndromal recovery 85.7%, functional recovery 32.6%. 29.0 (2.2 SE) mean days to 25% recovery. BP mixed: syndromal recovery 65.0%, functional recovery 47.4%. 30.0 (2.6 SE) mean days to 25% recovery. BP NOS: syndromal recovery 100.0%, functional recovery 55.6%. 38.0 (11.5 SE) mean days to 25% recovery. Psychosis NOS: syndromal recovery 72.4%, functional recovery 18.5%. 14.0 (2.3 SE) mean days to 25% recovery. Delusional disorder: syndromal recovery 71.4%, functional recovery 38.5%. 22.0 (15.9 SE) mean days to 25% recovery. Szform: syndromal recovery 100%, functional recovery 20.0%. 33.0 (15.9 SE) mean days to 25% recovery. SA: syndromal recovery 70.0%, functional recovery 0%. 31.0 (11.0 SE) mean days to 25% recovery. SZ: syndromal recovery 35.7%, functional recovery 15.4%. 65.0 (98.9 SE) mean days to 25% recovery. Syndromal recovery = no longer meeting criteria for illness. Functional recovery = return to premorbid level of vocational and residential functioning.	Diagnostic groups not compared
Williams[200] 1987 *Chestnut Lodge	PMD: Global functioning; 5% continuous incapacitation; 21% recovered. SA: Global functioning; 29% continuous incapacitation; 0% recovered. SZ: Global functioning; 41% continuous incapacitation; 6% recovered. BP: Global functioning; 32% continuous incapacitation; 11% recovered.	Diagnostic groups not compared
Angst[300] 1986 *Angst 86?	PMD congruent: 28% time in episode, median 4 episodes, median 5 months length of episodes, median 4.2 years length of cycle, 40% time in remission, 32% more than 5 years relapse free, 24% chronic course. N25 PMD incongruent: 21% time in episode, median 6 episodes, median 5.4 months length of episodes, median 5.1 years length of cycle, 19% time in remission, 35% more than 5 years relapse free, 21% chronic course. N48 NPMD: 19% time in episode, median 4 episodes, median 5.4 months length of episodes, median 4.6 years length of cycle, 33% time in remission, 48% more than 5 years relapse free, 7% chronic course. N100 NPBP: 18.4% time in episode, median 10 episodes, median 3.9 months length of episodes, median 2.2 years length of cycle, 24% time in remission, 25% more than 5 years relapse free, 12% chronic course. N72 PBP congruent: 15.3% time in episode, median 8.5 episodes, median 4.3 months length of episodes, median 3.8 years length of cycle, 45% time in remission, 40% more than 5 years relapse free, 5% chronic course. N20 PBP incongruent: 20% time in episode, median 10 episodes, median 4.2 months length of episodes, median 2.9 years length of cycle, 20% time in remission, 24% more than 5 years relapse free, 20% chronic course. N123	Diagnostic groups not compared
Brockington[301]	SAD: 23/75 (31%) failed to recover,	Diagnostic

Reference	Findings	Comparisons
1980	SZ: 35/53 (66%) failed to recover, PMD & PBP: 4/66 (6%) failed to recover	groups not compared
Angst[302] 1995a *Angst & Preisig 1995 papers	SAD: Median length of illness 23.6 years. Number of episodes = 6. Episodes per year = 0.19. Length of episode = 3.0 months. Length of cycles = 62 months. Time spent in illness = 15%. Length of last episode = 3.0 months. NPMD: Median length of illness 15.1 years. Number of episodes = 4. Episodes per year = 0.22. Length of episode = 5.6 months. Length of cycles = 54.3 months. Time spent in illness = 23%. Length of last episode = 4.0 months. NPBP: Median length of illness 25.0 years. Number of episodes = 10. Episodes per year = 0.37. Length of episode = 4.3 months. Length of cycles = 32.4 months. Time spent in illness = 19%. Length of last episode = 3.5 months. SAM: Median length of illness 29.7 years. Number of episodes = 11. Episodes per year = 0.35. Length of episode = 4.0 months. Length of cycles = 34.7 months. Time spent in illness = 19%. Length of last episode = 4.0 months. 181 examined retrospectively 225 examined prospectively	Diagnostic groups not compared
Coryell[303] 1987b *DST 6mo study	PMD: 17/29 (58.6%) recovered by follow-up; SAD: 18/46 (39.1%) recovered by follow-up; SZ: 2/20 (10.0%) recovered by follow-up; Congruence compared according to DSM-III	Diagnostic groups not compared
Welner[304] 1977	PMD: 6/64 episodic, 47/64 chronic, 11/64 indeterminable. Mania: 1/13 episodic, 7/13 chronic, 5/13 indeterminable. Depression and Mania: 0/13 episodic, 9/13 chronic, 4/13 indeterminable. Prominent affective symptoms: 2/20 episodic, 16/20 chronic, 2/20 indeterminable. few affective symptoms: 2/4 episodic, 2/4 chronic, 0/4 indeterminable.	Diagnostic groups not compared
Stephens[305] 1982	PMD: n10 long-term global follow-up mean 1.1 (1.1 SD), discharge status mean 1.5 (0.9). SZ: n 129 long-term global follow-up mean 2.0 (1.3 SD), discharge status mean 1.7 (1.0). SA: n 52 long-term global follow-up mean 1.6 (1.3 SD), discharge status mean 1.5 (0.9). Unspecified psychosis: n92 long-term global follow-up mean 1.2 (1.1 SD), discharge status mean 1.5 (1.1). Discharge status: 3 = unchanged; 2=slightly improved; 1=improved; 0=markedly improved. Global long-term follow-up: 0 = recovered, 1 = marked improvement, 2 = improved, 3 = slightly improved, 4 = deteriorated.	Statistics unclear
Aronson[203] 1987 *Aronson study	PMD: 35/42 had a recurrent course. PBP: 10/10 had a recurrent course.	Statistics unclear
Aronson[306] 1988a *Aronson study	PMD: 35/42 recurrent course, Of the recurrent, 7/35 reported episodes of non-delusional depression prior to index episodes but none after and 30/35 recurrent cases had only relapses of PMD. PBP: 10/10 relapsed with recurrent episodes of delusional depression, mania and mixed bipolar. 0/10 experienced nonpsychotic mania or NPMD prior to study. 10/10 had a recurrent course.	Statistics unclear

Reference	Findings	Comparisons
Goldberg[222] 2004 *Chicago follow-up study	PMD: Complete remission; 47% at 10 years, 35% at 7.5 years, 41% at 4.5 years and 27% at 2 years. BP: Complete remission; 41% at 10 years, 38% at 7.5 years, 47% at 4.5 years and 26% at 2 years. NPMD: Complete remission; 63% at 10 years, 63% at 7.5 years, 49% at 4.5 years and 40% at 2 years. Good outcome = adequate functioning with minimal or no symptoms, no hospitalisations and good work functioning.	Statistics unclear
Bromet[227] 1996 *Suffolk county	PMD: 50% had a full remission, 20% had a partial remission, 30% had new or original disorder (n 2 missing). SZ: 13.7% had a full remission, 34.7% had a partial remission, 51.6% had new or original disorder (n 1 missing). BP: 52.4% had a full remission, 17.5% had a partial remission, 30.2% had new or original disorder (n 1 missing).	Statistics unclear
Craig[307] 1997 *Suffolk county	PMD: 50% had a full remission, 20% had a partial admission, 30% had no remission. SZ: 13.7% had a full remission, 34.7% had a partial admission, 52.6% had no remission. BP: 52.4% had a full remission, 17.5% had a partial admission, 30.2% had no remission. Full remission = symptom free for at least 4 weeks (including positive and negative symptoms). Partial remission = having some symptoms but not meeting criteria for a full episode.	Statistics unclear
Charney[308] 1981	PMD: 39/54 (72%) had prior depressive episodes, mean 2.5 (2.33) prior episodes. 37/39 (95%) with recurrent illness had a previous episode of PMD. NPMD: 50/66 (76%) had prior depressive episodes, mean 2.52 (1.94) prior episodes 4/50 (8%) with recurrent illness had a previous episode of PMD.	Had prior depressive episodes: NPMD = PMD Mean prior depressive episodes: NPMD = PMD Recurrent illness: NPMD > PMD p<0.001
Copeland[172] 1983	PMD: 69% relapse at least once, 1.6 mean episodes of depression, 2.3 mean outcome. Retro: 1.6mean previous episodes. Neurotic depression: 44% relapse at least once, 0.6 mean episodes of depression, 3.1 mean outcome. Retro: 0.6mean previous episodes. (1-6, 1=recovered).	Relapse at least once: PMD = NPMD Episodes of depression: NPMD > PMD p<0.05 Mean outcome: NPMD > PMD p<0.05 Retrospective mean previous episodes: NPMD > PMD p<0.001
Frangos[72] 1983	PMD: 2.82 (0.16) mean episodes, 4mths 19 days average duration, 3y 3m 25d periodicity, 2 years 11 months 6 days duration of illness	Mean episodes:

Reference	Findings	Comparisons
	free intervals. NPMD: 3.05 (0.19) mean episodes, 4mths 1 day average duration, 3y 5m 19d periodicity, 3 years 1 months 18 days duration of illness free intervals.	NPMD = PMD Average duration: NPMD = PMD Periodicity & duration of illness free intervals: Not tested
Glassman[175] 1981	PMD: 1.1 (1.4 SD) previous episodes, 0/21 (0%) had a spontaneous remission within 2 weeks of psychosocial and placebo treatment. NPMD: 1.9 (1.8 SD) previous episodes, 18/60 (30%) had a spontaneous remission within 2 weeks of psychosocial and placebo treatment.	Previous episodes: NPMD = PMD Spontaneous remission: NPMD > PMD p<0.02
Hori[178] 1993	PMD: Course: remitting 5/38 (13%), intermitting 27/38 (71%), chronic 6/38 (16%). NPMD: Course: remitting 39/55(71%), intermitting 14/55(25%), chronic 2/55(4%).	Course: PMD = NPMD
Kessing[181] 2003	PMD: Median time to relapse = 2.6 years. All non PMD: Median time to relapse = 3.6 years.	Time to remission: NPMD > PMD p<0.05
Lenzi[182] 1996	PMD 3/11 (27%) had single episode. PMD recurrent: 7/8 had good recovery, 2.4 mean months of episode. PMD single episode: 4.7 mean months of episode. NPMD 9/39 (23%) had single episode. NPMD recurrent: 18/30 had good recovery, 7.1 mean months of episode. NPMD single episode: 6.4 mean months of episode. PBP-I: 17/22 had good recovery, 1.1 mean months of episode. NPBP-I: 34/44 had good recovery, 4.2 mean months of episode. PBP-II: 3/4 had good recovery, 2.5 mean months of episode. NPBP-II: 21/24 had good recovery, 6.4 mean months of episode.	Mean months in episode: Recurrent PMD > NPMD single episode PMD > NPMD PBP-I, NPBP-I, PBP-II, NPBP-II: Not tested
Leyton[183] 1995	PMD: Mean number of previous episodes was 3.4 (0.3). 22/25 had recurrent depression. 3/25 had only 1 episode of depression. Mean past episodes in recurrent patients was 3.7 (0.3). Median time from 1st to 2nd episode was 5.33 years. NPMD: Mean number of previous episodes was 1.4 (0.07). 44/120 had recurrent depression. 96/140 had only 1 episode of depression. Mean past episodes in recurrent patients was 2.4 (0.1). Median time from 1st to 2nd episode was 12.76 years.	Mean number of previous episodes: NPMD > PMD p<0.0001 Recurrent depression: NPMD > PMD p<0.0001 Only 1 episode of depression: NPMD > PMD p<0.0001 Mean past episodes in recurrent Ps: NPMD > PMD

Reference	Findings	Comparisons
		p<0.0001 Median time from 1st to 2nd episode: NPMD > PMD p<0.0002
Lykouras[184] 1994	PMD: 9/32 (28%) did not fully recover at all over the follow-up. Mean 1.74 (1.3) depressive episodes per patient. 6/32 with a chronic course. 9/32 had a major depressive episode by the end of follow-up. 64 total depressive episodes, 49 psychotic, 15 not psychotic. NPMD: 6/41 (15%) did not fully recover at all over the follow-up. Mean 2.22 (1.06) depressive episodes per patient. 5/41 with a chronic course. 12/41 had a major depressive episode by the end of follow-up. 91 total depressive episodes, 13 psychotic, 78 not psychotic.	Not fully recovered: PMD = NPMD Mean depressive episodes: PMD = NPMD Chronic course: PMD = NPMD Major depressive episode by the end of follow-up: PMD = NPMD Total depressive episodes: NPMD > PMD p<0.001
Parker[309] 1991	PMD: 17% (6/35) had a clear and persisting remission, 26% (9/35) had incomplete remission or relapse, 57% (20/35) had a slight or transitory improvement. NPMD: 31% (11/35) had a clear and persisting remission, 46% (16/35) had incomplete remission or relapse, 23% (8/35) had a slight or transitory improvement.	Remission: PMD=NPMD
Robinson[189] 1985	PMD: clinical status over the first year – asymptomatic 22/52, chronically ill 15/52, episodically ill 13/52, other/ unknown/dead 2/52. NPMD: clinical status over the first year – asymptomatic 32/52, chronically ill 3/52, episodically ill 14/52, other/ unknown/dead 3/52. Chronically ill = patient being symptomatic of either psychosis only or a major depressive episode with or without delusions continuously for 9 months or longer during the follow-up period. Episodically ill = episodes of psychosis or major depression lasting less than 9 months.	Asymptomatic: NPMD > PMD p=0.05 Chronically ill: NPMD > PMD p=0.002 Episodically ill: PMD = NPMD other/ unknown/dead PMD = NPMD
Maj[199] 1990 *Naples overlapping samples	PMD mood congruent: Number of episodes at 7 years; NPMD 22, 37%; PMD congruent 29, 48%; PMD incongruent 4, 7%; other 5, 8%. NPMD: Number of episodes at 7 years; NPMD 47, 80%; PMD congruent 8, 13%; PMD incongruent 1, 2%; other 3, 5%.	Frequency of various episode types: NPMD > PMD p<0.01.
Winokur[310]	PMD: 3 episodes.	Episodes:

Reference	Findings	Comparisons
1985 *Angst 86?	NPMD: 3 episodes. PBP: 4.5 episodes. NPBP: 4 episodes.	PMD = NPMD PBP & NPBP not test
Coryell[311] 1986b *Coryell 86	PMD: 17/46 recovered narrow, 24/46 recovered broad, 32.2 mean weeks without depressive symptoms, 36.3 mean weeks with full depressive symptoms. NPMD: 41/159 recovered narrow, 91/159 recovered broad, 20.6 mean weeks without depressive symptoms, 32.5 mean weeks with full depressive symptoms. Narrow recovered = a minimum of 8 week period with no criteria symptoms at all. Broader recovered = no more than 1 or 2 symptoms to a mild degree for the best 8 week period.	All outcomes: PMD = NPMD
Winokur[210] 1992 *IOWA 70-81	PMD congruent: 31% (24/76) no relapse. PMD incongruent: 52% (31/60) no relapse. NPMD: 50% (302/604) no relapse. NPBP: relapse not reported. PBP congruent: relapse not reported. PBP incongruent: relapse not reported.	PMD = NPMD NPBP & PBP not tested
Coryell[312] 1982a *IOWA 500	PMD: Condition at discharge: recovered 34/121, improved 23/121, unimproved 64/121, discharged to community 46/121. Short term follow-up: 3.4yrs, Recovered 51/108, improved 23/108, unimproved 34/108. NPMD: Condition at discharge: recovered 47/102, improved 18/102, unimproved 37/102, discharged to community 63/102. Short term follow-up: 5.0 years, Recovered 69/95, improved 7/95, unimproved 19/95.	Recovered at discharge: NPMD > PMD p<0.025 Improved: PMD=NPMD Unimproved: PMD=NPMD Discharged to community: NPMD > PMD p<0.001 Short term follow-up: 3.4yrs, Recovered: NPMD > PMD p<0.005 Improved: PMD=NPMD Unimproved: PMD=NPMD
Coryell[313] 1982b *IOWA 500	2-3 years: PMD congruent: recovered 46.3%, improved 31.6% PMD incongruent: recovered 39.8%, improved 31.8%. Recovery at 5 year follow-up: PMD congruent: 76.5% PMD incongruent: 71.4% 2-3 years for non-somatic therapies only: NPMD: recovered – 69.2%, improved – 10.3%, unimproved 21.8% PMD congruent: recovered – 43.7%, improved – 21.1%, unimproved	2-3 years for non-somatic therapies only: NPMD > Congruent PMD p<0.05 Congruent PMD > SZform & SZ

Reference	Findings	Comparisons
	35.2% PMD incongruent: recovered – 32.6%, improved – 32.6%, unimproved 34.9% Szform: recovered – 16.6%, improved – 18.8%, unimproved 64.6% Sz: recovered – 7.0%, improved – 15.8%, unimproved 77.2% Recovery defined as returned to premorbid level of functioning and had a complete remission of symptoms. Improved defined as returned to usual occupation without remission or remitted without returning to premorbid functioning Unimproved defined as everyone else	p<0.05 NPMD > Incongruent PMD p<0.05 Incongruent PMD > SZform & SZ p<0.05 Congruent PMD = incongruent PMD All others not tested.
Coryell[314] 1987a *NIMH collaborative depression study	PMD: 6mths: 53% recovered from index episode. 2 years: 75% recovered from index episode. Of the 14/55 patients who did not recover by 2 years, 64% had no partial recovery while 36% did have partial recovery. Of those 41/55 who recovered by 2 years, 76% had complete recovery, 24% had an incomplete recovery, 29% had no subsequent episode, 44% had only 1 subsequent episode and 7% had more than 1 other episode. Median time to recovery = 26.3 weeks. NPMD: 6mths: 58% recovered from index episode. 2 years: 83% recovered from index episode. Of the 78/451 patients who did not recover by 2 years, 39% had no partial recovery while 55% did have partial recovery. Of those 373/451 who recovered by 2 years, 72% had complete recovery, 28% had an incomplete recovery, 19% had no subsequent episode, 32% had only 1 subsequent episode and 13% had more than 1 other episode. Median time to recovery = 18.5 weeks. Recovery = a cross sectional judgement – not sustained recovery. Recovery at 6 months = minimum 8 consecutive weeks with no more than ½ depression symptoms of mild intensity.	All outcomes: PMD = NPMD
Goldberg[223] 2005 *Chicago follow-up study	PMD: 6/17 (35%) high-moderate, sub threshold or full major depressive syndrome was present. BP: 9/30 (30%) high-moderate, sub threshold or full major depressive syndrome was present. NPMD: 24/77 (31%) high-moderate, sub threshold or full major depressive syndrome was present.	PMD = BP PMD = NPMD
Sands[225] 1994 *Chicago follow-up study	PMD: follow-up year: 6/31 remitted, 14/31 had subsyndromal depression, 11/31 had the full syndrome. 11/31 had no signs of psychosis, 7/31 had suspected signs of psychosis, 13/31 had definite signs of psychosis. NPMD: follow-up year: 18/63 remitted, 24/63 had subsyndromal depression, 21/63 had the full syndrome. 53/63 had no signs of psychosis, 3/63 had suspected signs of psychosis, 7/63 had definite signs of psychosis.	Depression: NPMD = PMD Psychosis: NPMD > PMD p<0.001 Remission: unclear
Coryell[216] 1997 *NIMH collaborative depression	PMD: mean of 102.2 (114.9 SD) weeks in full syndrome. NPMD: mean of 66.8 (84.0 SD) weeks in full syndrome.	Weeks in syndrome: NPMD > PMD

Reference	Findings	Comparisons
study		
Coryell[236] 1988	SAD: 6 months: recovered from depressive syndrome 27.6%, recovered from psychosis with insight 27.6%, 62.1% with no partial remission. 12 months: recovered from depressive syndrome 41.4%, recovered from psychosis with insight 37.9%, 51.7% with no partial remission. SABP: 6 months: recovered from depressive syndrome 28.6%, recovered from psychosis with insight 64.3%, 42.9% with no partial remission. 12 months: recovered from depressive syndrome 64.3%, recovered from psychosis with insight 78.6%, 28.6% with no partial remission.	6 months: Recovered from depressive syndrome: SAD = SABP Recovered from psychosis with insight: SABP > SAD $p<0.05$ No partial remission: SAD = SABP 12 months: Recovered from depressive syndrome SAD = SABP Recovered from psychosis with insight: SABP > SAD $p<0.05$ No partial remission: SAD = SABP
Kendler[239] 1995	SAD: Mean (SD) Levels of functioning scale - Course 2.9 (0.8). Duration of illness - 70 months (90 SD). SABP: Mean (SD) Levels of functioning scale – Course 2.8 (0.4). Duration of illness - 70 months (78 SD). SZ: Mean (SD) Levels of functioning scale – Course 3.4 (0.8). Level of functioning 1 (poor) – 5 (good).	Levels of functioning: SAD = SABP Duration of illness: SAD = SABP No comparisons to schizophrenia.
Maj[242] 1985 *Naples overlapping samples	SAD: RETROSPECTIVE - Mean duration of illness 7.2 years (5.8), mean episodes per year 0.5 years (0.3), PROSPECTIVE – 1.3 (1.1) mean morbid episodes, 2.1 (1.9) total months morbidity, SAM: RETROSPECTIVE - Mean duration of illness 9.8 years (3.1), mean episodes per year 0.6 years (0.3), PROSPECTIVE – 0.9 (1.5) mean morbid episodes, 1.1 (1.4) total months morbidity, 0.4 (0.6) mean hospitalisations, NPMania: RETROSPECTIVE - Mean duration of illness 8.5 years (3.8), mean episodes per year 0.5 years (0.2), PROSPECTIVE – 0.8 (1.4) mean morbid episodes, 0.8 (1.4) total months morbidity, 0.4 (0.6) mean hospitalisations. NPMD: RETROSPECTIVE - Mean duration of illness 9.6 years	Duration of illness: SAD = NPMD Episodes per year: SAD = NPMD morbid episodes: SAD = NPMD Morbidity months: NPMD > SAD $p<0.05$

Reference	Findings	Comparisons
	(4.5), mean episodes per year 0.5 years (0.2), PROSPECTIVE – 0.8 (0.9) mean morbid episodes, 1.0 (1.2) total months morbidity.	SAD vs. SAM & NPMania not tested
Angst[315] 1995b *Angst & Preisig 1995 papers	SAD: 24% recovered, 10% chronic. NPMD: 26% recovered, 14% chronic. SABP: 16% recovered, 19% chronic. NPBP: 16% recovered, 12% chronic.	Chronic: SAD = NPMD Recovery not compared. SAD not compared with SABP & NPBP
Marneros[316] 1988a *Cologne study	SAD: 3.36 mean episodes, 3 median episodes. Annual frequency of episodes mean 0.13, 0.12 median episodes. Annual frequency of cycles mean 0.23, median 0.25. SABP: 5.46 mean episodes, 6 median episodes. Annual frequency of episodes mean 0.26, 0.28 median episodes. Annual frequency of cycles mean 0.40, median 0.48.	Median episodes: SAD > SABP p=0.007 Annual frequency of episodes: SAD > SABP p<0.000 Annual frequency of cycles: SAD > SABP p=0.011
Marneros[317] 1988b *Cologne study	SAD: Average cycle length mean 35.59 months, median 45.5. SABP: Average cycle length mean 22.52 months, median 26.1.	SABP > SAD p=0.033
Marneros[318] 1988c *Cologne study	SAD: Median inactivity period of 19 months. SABP: Median inactivity period of 9 months.	SABP > SAD p=0.018
Marneros[319] 1989b *Cologne study	SAD: median 3, mean 4.33 (3.41) episodes, annual frequency of episodes median 0.12 mean 0.16 (0.11), number of cycles median 2, mean 3.87 (3.38), annual frequency of cycles median 0.25 mean 0.34 (0.32). Average length of cycles median 45.5 mean 74.07 (62.15), average length of episode per patient 2.42 median months 2.77 (2.18) mean months, average length of intervals per patient 43.5 median months, 69.24 (59.40) mean months. SABP: median 6, mean 6.88 (4.36) episodes, annual frequency of episodes median 0.28 mean 0.35 (0.27), number of cycles median 6, mean 6.44 (4.15), annual frequency of cycles median 0.48 mean 0.51 (0.33). Average length of cycles median 26.07 mean 40.21 (33.49), average length of episode per patient 1.75 median months 2.09 (1.34) mean months, average length of intervals per patient 22.97 median months, 37.65 (33.58) mean months.	Number of episodes: SAD > SABP p=0.007 Annual freq of episodes: SAD > SABP p<0.000, Number of cycles: SAD > SABP p=0.002, Annual freq of cycles: SAD > SABP p=0.011. Average length of cycles: SABP > SAD p=0.033,

Reference	Findings	Comparisons
		Average length of episode: SAD = SABP Length of intervals: SABP > SAD p=0.045
Marneros[320] 1990a *Cologne study	SAD: polyphasic course 42.2%, activity of illness mean 13.3 years (11.2 s.d.), inactivity of illness mean 16.6 years (9.3 s.d.). NPMD: polyphasic course 46.1%, activity of illness mean 15.9 years (12.8 s.d.), inactivity of illness mean 15.6 years (7.1 s.d.) SABP: polyphasic course 75.0%, activity of illness mean 15.7 years (10.9 s.d.), inactivity of illness mean 11.7 years (7.9 s.d.). NPBP: polyphasic course 66.7%, activity of illness mean 15.3 years (11.7 s.d.), inactivity of illness mean 12.3 years (6.4 s.d.).	polyphasic course: SAD = NPMD Activity of illness mean: SAD = NPMD Inactivity of illness: SAD = NPMD No other comparisons made to SAD
Marneros[321] 1990b *Cologne study	Reported above.	
Tsuang[259] 1993	Mood congruent PMD: recovered from psychosis: 10/17 (58.8%) Mood incongruent PMD: recovered from psychosis: 4/15 (26.7%) SAD: recovered from psychosis: 0/11 (0%) Schizophrenia: recovered from psychosis: 0/22 (0%)	Recovery: Mood congruent PMD > SAD Mood congruent PMD > SZ Combined PMD > SAD Combined PMD > SZ SAD and SZ not compared.
Sands[262] 1999 *Chicago follow-up study	PMD: No depression in follow-up 5/17 (29%). SAD: No depression in follow-up 9/31 (29%), SZ: No depression in follow-up 17/70 (24%). NPMD: No depression in follow-up 25/69 (36%).	PMD = SAD = SZ = NPMD
Brockington[322] 1982	PMD/SAD mixed CATEGO PMD: 11/16 had persistent depression, 0.89 mean episodes / year, 3.0 mean schizoaffective episodes, 1.8 mean PMD episodes, 6/16 with at least 1 schizoaffective episode. Neurotic depression: 6/20 had persistent depression, 0.59 mean episodes / year, 2.0 mean schizoaffective episodes, 0.7 mean PMD episodes, 1/20 with at least 1 schizoaffective episode. Retarded depression: 6/18 had persistent depression, 0.38 mean episodes / year, 1.1 mean schizoaffective episodes, 0.5 mean PMD episodes, 2/18 with at least 1 schizoaffective episode. RDC	CATEGO Persistent depression: Neurotic & retarded depression > PMD p<0.05 Mean episodes / year: Neurotic & retarded

Reference	Findings	Comparisons
	PMD: 6/55 failed to recover, 12/55 with at least 1 schizophrenic symptom, 4/55 with at least 1 schizophrenic episode, 9/55 with at least 1 SA episode. SAD: 6/11 failed to recover, 9/11 with at least 1 schizophrenic symptom, 9/11 with at least 1 schizophrenic episode, 6/11 with at least 1 SA episode. DSM - combo vs. NPMD PMD Mood congruent: 7/11 with at least 1 SA episode, 2/11 failed to recover. PMD Mood incongruent: 8/14 with at least 1 SA episode, 7/14 failed to recover. NPMD: 2/45 with at least 1 SA episode, 4/45 failed to recover.	depression > PMD p<0.05 Mean schizoaffective episodes: Neurotic & retarded depression > PMD p<0.01 Mean PMD episodes: Neurotic & retarded depression > PMD p<0.0001 At least 1 schizoaffective episode: Neurotic & retarded depression > PMD p<0.05 RDC Failed to recover: PMD > SAD p<0.01 At least 1 schizophrenia symptoms: PMD > SAD p<0.001 At least 1 schizophrenia episode: PMD > SAD p<0.05 At least 1 SA episode: PMD > SAD p<0.05 DSM: SA episode: NPMD > PMD combo p<0.05 Failed to recover:

Reference	Findings	Comparisons
		NPMD > PMD combo p<0.01
Winokur[267] 1996 *DST 6 month study	Recovered: PMD/SAD 18/22 (81.8%) Schizophrenia 6/29 (20.7%) Unstable diagnoses group 5/18 (27.8%).	Recovery: PMD/SAD > SZ p=0.00001 PMD/SAD > Unstable diagnoses group p=0.001

< means worse than; > means better than; = means equivalent outcomes
SZ = schizophrenia; BP = bipolar disorder; SA = schizoaffective disorder (general); Szform = schizophreniform; NPMD = non-psychotic major depression; NPBP = non-psychotic bipolar disorder; PBP = psychotic bipolar disorder; SABP = schizoaffective disorder bipolar type; SAM = schizoaffective disorder manic type; NPMania = non-psychotic mania.

4.4.2.3. Mortality and suicidality

Of the 103 papers identified for this review, 35 had data on a mortality or suicidality related outcome. Twenty papers reported on mortality, 18 on completed suicide, 12 on suicide attempts and 3 on suicidal ideation. Of the 35 papers, 28 were on PMD, 4 were on SAD, 2 were on PMD and SAD and 1 was on PMD/SAD mixed together.

4.4.2.3.1. Mortality

Of the 19 papers which reported on mortality (presented in Table 4-6) only 18 contained useable data. One paper combined PMD and SAD cases into the same group making interpretation of the findings difficult but also provided no comparison groups.

Of the remaining 17 papers, only three report on PMD and schizophrenia cases within the same study. Two of these are long-term studies and both report a higher percentage of PMD cases died over the follow-up (43-78% versus 42%;[323] and 34% versus 19%[258]). The one paper which reports similar death rates (10% in each group) was based on only a one year follow-up study.[1] One study reports on deaths in SAD and schizophrenia cases, and reports 67% of SAD cases were dead at 28-32 year follow-up compared with

19% of schizophrenia cases.[258] Although none of these studies compare the groups statistically, the findings indicate that over the long-term, death rates may be higher in PMD and SAD cases compared with schizophrenia cases.

Four papers reported on PMD and bipolar cases within the same study. Three of these papers indicated that PMD cases had more deaths compared with bipolar cases even though one study was only a two year follow-up (10-20% versus 3-6%[210]) and the other two were long term follow-ups (0-14 years (11% versus 6-8%)[209] and 10 year (8% versus 3%)[230]). The fourth study had overlapping percentages of deaths (12-15% in PMD versus 5-18% in bipolar disorder). None of these studies compared PMD and bipolar statistically but the trend from these studies indicate that PMD cases may have higher death rates compared with bipolar cases. One study reported on deaths in SAD and bipolar cases and reports 63% of SAD cases were dead at 28-32 year follow-up compared with 70% of bipolar cases.[324] Again, this difference was not statistically tested.

Within these studies on mortality, there were two papers based on incidence studies[1, 197] but these do not report on long-term mortality. There are 10 long-term studies, but none of these are incidence studies. This indicates a need for long-term incidence studies.

Based on the trends discussed above, from the current literature, it was hypothesized that PMD and SAD cases would have a higher proportion of cases who die (from all causes) over the follow-up period compared with schizophrenia and bipolar cases.

Table 4-6: Mortality

Paper	Time period	PMD	SAD	PMD /SAD mixed	NPMD	Schizophrenia	BP	Other	Statistical tests
Coryell[325] 1982a *IOWA 500	20 years	unclear			unclear			Denominators unclear	None
Whitty[197] 2005	4 years	0%							-
Pederson[326] 1972	5 years	16%						no comparison	-
Angst[327] 1986 *Angst 86?	17-21 years	12-15%			9%		5-18%		None
Maj[185] 2007	10 years	7.9%			5%			5.7% (Depression with preoccupations)	chi2=0.98, df=2, p<0.06
Parker[328] 1991	1 year	3%			0%				None
Robinson[189] 1985	1 year	2%			0%				p=n/s
Winokur[210] 1992 *IOWA 70-81	2 years	10-20%			14%		3-6%		None
Black[209] 1988 *IOWA 70-81	0-14 years	11%			12%		6-8%		None
Copeland[172] 1983	5 years	12%			14%				"no significant differences"
Lykouras[184] 1994	6 years	3%			5%				None
Vythilingham[329] 2003	15 years	41%			20%				x2=3.99, df=1, p<0.05
Suominen[193] 2009	4.2 years	2.48 RRR			0.83-1.17 RRR				None
Coryell[330]	40 years	43-78%			67%	42%		43%	None

Paper	Time period	PMD	SAD	PMD /SAD mixed	NPMD	Schizophrenia	BP	Other	Statistical tests
1985 *IOWA 500								(Szform)	
Craig[230] 2006 *Suffolk county	10 years	7.9%					2.8%	4% (other psychoses) 5.1% (mixed SZ/SA/Szform)	unclear
Crebbin[1] 2008	1 year	10%				10%			None
Opjordsmoen[258] 1989	3-39 years	34%	67%			19%			None
Angst[331] 1995a *Angst & Preisig 1995 papers	22-26 years 28-32 years		40.8% 63.3%		62.8% 70.8%		53.8% 69.8%	44.7% (SAM) 50.9% (SAM)	Overall = p<0.01 Overall = p<0.005
Coryell[266] 2008 *DST 6 month study	17 years			24%					None

SZ = schizophrenia; BP = bipolar disorder; SA = schizoaffective disorder (general); Szform = schizophreniform; NPMD = non-psychotic major depression; SAM = schizoaffective disorder manic type; n/s = non significant.

4.4.2.3.2. Completed suicides

Eighteen papers reported on completed suicide, 17 of which had useable data. Table 4-7 shows the findings from the 17 papers that report on completed suicides. Only two studies report on completed suicide in schizophrenia and PMD cases within the same study.[190, 200] Both studies report that more PMD cases had a completed suicide compared with schizophrenia cases (6/39 PMD cases versus 4/39 cases;[190] 18% versus 8%[200]). However, one study did not conduct statistical tests on the PMD-schizophrenia comparison and the other found no differences between the groups. Although both of these papers are based on long-term studies, neither of them are based on incidence samples. No papers reported on SAD and schizophrenia cases. Although not statistically significant or not statistically tested, the evidence indicates that completed suicide may be higher in PMD cases (and SAD cases as PMD and SAD is similar in terms of symptoms) compared with schizophrenia cases.

Six papers reported on PMD and bipolar disorder[190, 200, 209, 210, 230, 332] and all except one[190] report that PMD cases has higher percentages of completed suicides.[200, 209, 210, 230, 333] However, all of these studies either reported no statistical difference between PMD and bipolar disorder or did not report any statistics. Only one study reported on SAD cases compared with bipolar cases. This paper reported that 8% of cases completed suicide over a 27 year follow-up compared with 7% in bipolar cases (no statistical tests were conducted).[334] Although not statistically significant, or even tested in some cases, the evidence indicates a trend that completed suicide may be higher in PMD and SAD cases compared with bipolar cases.

Table 4-7: Completed suicides

Paper	Time period	PMD	SAD	PMD/SAD mixed	NPMD	Schizophrenia	BP	Other	Statistical tests
Pederson[335] 1972	5 years	2%						No comparison	-
Parker[336] 1991	Time scale not reported	2.86%			0%				None
Robinson[189] 1985	1 year	2%			0%				p=n/s
Maj[185] 2007	10 years	12%			1%			2% (Depression with preoccupations)	None
Kessing[181] 2003	1-6 years	1.5%			1.8%				p=0.6
Coryell[337] 1982a *IOWA 500	20 years	8%			10%				None
Angst[338] 1986 *Angst 86?	17-21 years	8-10%			11%		0-9%		None
Black[209] 1988 *IOWA 70-81	0-14 years	3%			3%		1-2%		no significant difference
Vythilingham[339] 2003	15 years	8%			8%				p=n/s
Wolfersdorf[198] 1987	retrospective	9%			4%				p=n/s
Winokur[210] 1992 *IOWA 70-81	2 years	5%			4%		0-1%		p=n/s
Suominen[193] 2009	4.2 years	7.56 RRR			1-3.1 RRR				None
Roose[190] 1983	retrospective	5.3 OR raw			1 OR raw numbers:	raw numbers: 4/39	raw numbers: 8/39	raw numbers: PD 2/39	overall p<0.05

Paper	Time period	PMD	SAD	PMD/SAD mixed	NPMD	Schizophrenia	BP	Other	Statistical tests
		numbers: 6/39			4/39			Other 3/39	
Craig[230] 2006 *Suffolk county	10 years	2%					0%	SZ/SA/Szform: 2% Other psychosis: 2%	unclear
Williams[200] 1987 *Chestnut Lodge	2-32 years	18%				8%	0%	SA 10%	p=n/s
Angst[340] 1995b *Angst & Preisig 1995 papers	27 years		8%		15%		7%	SABP 10%	None
Coryell[266] 2008 *DST 6 month study	17 years			7%				No comparison	-

SZ = schizophrenia; BP = bipolar disorder; SA = schizoaffective disorder (general); Szform = schizophreniform; NPMD = non-psychotic major depression; SABP = schizoaffective disorder bipolar type; n/s = non significant.

4.4.2.3.3. Suicide attempts

Suicide attempts were reported in 12 papers but only 11 had useable data (see Table 4-8). There was very little research on suicide attempts comparing PMD cases to schizophrenia and bipolar disorder cases and no data on SAD cases. There were also no incidence based studies and only one long-term study, the others being based on short-medium term studies or retrospective case reviews. Only one paper reported on PMD and schizophrenia within the same study: Radomsky et al.[188] examined attempted suicide rates in PMD compared with schizophrenia, schizoaffective disorder general and other psychoses. They reported that 42% of PMD cases had attempted suicide in their lifetime compared with 27% of schizophrenia cases (however, this was not tested statistically).[188] Therefore, it was hypothesized that PMD cases would be more likely to attempt suicide compared with schizophrenia cases.

Two papers compared attempted suicide rates for PMD with bipolar disorder. Winokur et al.[210] reported 3-4% of PMD cases compared with 1-10% of bipolar cases attempted suicide over a 2 year follow-up. Radomsky et al.[188] in their review of case notes reported that 42% of PMD cases and only 26% of bipolar cases had ever attempted suicide in their lifetime. However, neither result was statistically tested. The difference in findings could be due here to data collection differences (retrospective case notes review versus prospective study) or the follow-up time difference (retrospective versus 2 year follow-up). However, based on the hypotheses from section 4.4.2.3.2, that PMD cases are more likely to complete suicide than bipolar cases, it was hypothesized that PMD cases are more likely to attempt suicide compared with bipolar cases.

Table 4-8: Suicide attempts

Reference	Time period	PMD	SAD	PMD/ SAD mixed	NPMD	Schizophrenia	BP	Other	Statistical tests
Robinson[189] 1985	1 year	4%			2%				p=n/s
Wolfersdorf[198] 1987	retro	37%			20%				p=n/s
Frangos[72] 1983	retro	27.6%			22.7%				p=n/s
Maj[185] 2007	10 year	27%			18%				p=n/s
Frances[341] 1981	missing	3%			18%				p=n/s
Johnson[73] 1991	1 year	0%			0.4%				p=n/s
Winokur[210] 1992 *IOWA 70-81	2 years	3-4%			5%		1-10%		p=n/s
Miller[207] 1987 *Miller papers	retro	51%			34%				p=n/s
Miller[208] 1988 *Miller papers	reported above								
Hori[178] 1993	retro	47%			18%				p<0.05
Suominen[193] 2009	4.2 years	1.25 RR			1-1.77 RR				None
Radomsky[188] 1999	retro	42%				27%	26%	SA 43% Other 25%	None

SZ = schizophrenia; BP = bipolar disorder; SA = schizoaffective disorder (general); NPMD = non-psychotic major depression; n/s = non significant.

4.4.2.3.4. Self-harm

Only one paper reported on self-harm in PMD or SAD cases.[1] This paper reported that 33% of PMD cases self-harmed compared with 18% of schizophrenia cases ($p<0.01$).[1] This study was a one year follow-up of an incidence sample. Therefore longer term studies are needed to examine the long term outcomes for PMD cases in terms of self-harm. However, based on this single study, it was hypothesized that PMD and SAD cases (due to the similarity between the diagnoses) would be more likely to self-harm compared with schizophrenia and bipolar cases.

4.4.2.4. Psychosocial functioning

Of the 103 papers identified for this review, 30 had data on psychosocial outcomes. Of these, 14 were on PMD, 9 were on SAD, 5 were on PMD and SAD and 2 were on PMD/SAD mixed. The papers on psychosocial outcomes report on a wide range of outcomes: social network and relationship related outcomes (e.g. social status, marital status, living situation, social functioning / contacts, autarky); employment related outcomes (e.g. employment, activities and financial dependence); psychologically related outcomes (e.g. satisfaction, motivation, self-harming); disability and major illness; and overall functioning (e.g. Global Assessment of Functioning, Global Assessment Scale). Within this review, the following areas have been focussed on as they will be the focussed on in the results of the thesis due to available data: employment; relationship status; social contacts; and prison time.

4.4.2.4.1. Employment outcomes

Seventeen papers reported on occupation related papers (these are author defined; Table 4-9). Of the eight papers which examined PMD, five compared it to schizophrenia. All

five papers reported that PMD groups had better employment outcomes compared with schizophrenia groups,[180, 227, 258, 259, 262] and this was a statistical difference in five out of the seven comparisons[180, 258, 259, 262] (one was not compared statistically[227] and one had no difference[262]). Four papers compared SAD to schizophrenia, all of which found SAD cases to have better outcomes compared with schizophrenia cases.[239, 258, 259, 262] However, this was a statistical difference in only one out of the four comparisons[258] as one study did not compare the groups statistically[239] and two others found no statistical difference between SAD and schizophrenia cases.[259, 262]

Only two studies compared PMD cases with bipolar disorder cases. One of these papers reported that 75% of PMD cases did not work for three out of the six month follow-up compared with 71% of bipolar cases but this was not statistically compared.[227] The other study only reported on work satisfaction rather than actual employment outcomes.[223] There were no studies comparing SAD to bipolar disorder.

Based on the literature discussed above, it was hypothesized that PMD and SAD cases would have a higher proportion of cases who were employed over follow-up compared with schizophrenia cases.

Table 4-9: Occupation outcomes

Reference	Finding	Statistical comparisons
Van Praag[264] 1984	Schizophrenia (n): Occupational level 1 (n11, 26%); 2 (n20, 48%); 3 (n4, 10%); 4 (n4, 10%); 5 (n3, 7%). Average 2.2. (no standard deviations) SA melancholic (n): Occupational level 1 (n10, 83%); 2 (n2, 17%); 3 (n0); 4 (n0); 5 (n0). Average 1.2. (no standard deviations) SAD/PMD mixed (n): Occupational level 1 (n4, 33%); 2 (n3, 25%); 3 (n4, 33%); 4 (n1, 8%); 5 (n0). Average 2.2. (no standard deviations) SA manic congruent (n): Occupational level 1 (n4, 57%); 2 (n3, 43%); 3 (n0); 4 (n0); 5 (n0). Average 1.4. (no standard deviations) SA manic incongruent (n): Occupational level 1 (n3,	Unclear

Reference	Finding	Statistical comparisons
	30%); 2 (n4, 40%); 3 (n2, 20%); 4 (n1, 1%); 5 (n0). Average 2.1. (no standard deviations) NPMD (n): Occupational level 1 (n19, 66%); 2 (n7, 24%); 3 (n2, 7%); 4 (n1, 3%); 5 (n0). Average 1.5. (no standard deviations) NPBP (n): Occupational level 1 (n12, 57%); 2 (n7, 33); 3 (n1, 5%); 4 (n1, 5%); 5 (n0). Average 1.6. (no standard deviations) The paper reports p<0.01 but it is unclear between which diagnostic comparisons the differences lie. Occupational level: Higher score indicates higher dysfunction.	
Bromet[227] 1996 *Suffolk county	PMD: 75% did not work for more than 3 months out of 6 in follow-up. BP: 71% did not work for more than 3 months out of 6 in follow-up. SZ: 87.4% did not work for more than 3 months out of 6 in follow-up, Overall P<0.05 but unclear between which diagnoses.	Unclear
Maj[199] 1990 *Naples overlapping samples	PMD mood congruent: Mean DAS; household acts 1.0 (0.6SD); work performance 0.8 (0.8 SD). NPMD: Mean DAS; household acts 1.1 (0.5 SD); work performance 0.9 (0.7 SD). DAS: higher scores indicate higher levels of disability.	No statistical comparisons
Brockington[342] 1982	PMD: 31.2 mean employment score. SAD: 43.0 mean employment score. Higher scores indicate poorer adjustment.	Employment score: PMD > SAD p<0.05
Coryell[236] 1988	SAD: 69.0% missed more than 5 weeks of work due to psychopathology. SABP: 64.3% missed more than 5 weeks of work due to psychopathology.	Missed work: SAD = SABP
Coryell[343] 1987a *NIMH Collaborative Study for the Affective Disorders	PMD: 9/32 (28%) had mild-severe work impairment at 2 yrs. NPMD: 99/325 (30%) had mild-severe work impairment at 2 yrs.	Work impairment: NPMD = PMD
Jager[180] 2005	PMD: 78.9% in regular employment. NPMD: 78.1% in regular employment. SZ: Mean: 46.9% in regular employment.	Regular employment: NPMD = PMD p=0.945 PMD > SZ, p=0.014
Johnson[73] 1991	PMD: 27.4% welfare or disability. NPMD: 11.2% welfare or disability.	Welfare or disability: NPMD > PMD p<0.001
Kendler[239] 1995	SAD: Mean (SD) Levels of functioning scale – quantity of useful work 3.3 (1.5), quality of useful work 2.9 (1.2). Affective illness: Mean (SD) Levels of functioning scale – quantity of useful work 3.7 (1.3), quality of useful work 3.5 (1.0). SABP: Mean (SD) Levels of functioning scale – quantity of useful work 2.8 (1.1), quality of useful work 3.0 (1.1). SZ: Mean (SD) Levels of functioning scale –quantity of useful work 1.9 (1.1), quality of useful work 2.0	Unclear between SAD and affective illness and schizophrenia. SAD = SABP p<0.05

Reference	Finding	Statistical comparisons
	(1.1). Higher score indicates better outcome	
Marneros[344] 1989c *Cologne study	SAD: Occupational drift: down 24%, 9/37, none 76% 28/37. Premature retirement: 5/22 23%. SABP: Occupational drift: down 38%, 13/34, none 62% 21/34. Premature retirement: 8/27 30%. GAS: Higher score indicates better adjustment	Occupational drift, down: SABP = SAD p=0.2054 Premature retirement: SABP = SAD p=0.5862
Marneros[345] 1990a *Cologne study	SAD: Downward occupational drift 29%, premature retirement 19.4%. NPMD: Downward occupational drift 29%, premature retirement 25.8%. SABP: Downward occupational drift (20/38) 52.6%, premature retirement (12/38) 31.6%.	Downward occupational drift: SAD = NPMD p=1.000 Premature retirement: NPMD = SAD p=0.544 No comparisons between SAD and SABP
Marneros[346] 1990b *Cologne study	Reported above.	-
Opjordsmoen[258] 1989	PMD: mean employment score 3.5 (0.9), employed or receiving pension 69%. SAD: mean employment score 2.7 (1.4), employed or receiving pension 46%. SZ: mean employment score 1.3 (1.5), employed or receiving pension 20%. Employment: higher score indicates better adjustment.	Employment score: PMD > SZ p<0.001 SAD > SZ p<0.01 PMD < SAD p<0.01 Employment or receiving pension: PMD > SZ p<0.001 SAD > SZ p<0.05 PMD = SAD
Goldberg[223] 2005 *Chicago Follow-up Study	PMD: Mean Life satisfaction at 7-8 years, work 2.0 (0.8 SD), economic 2.9 (1.3 SD). 4.5 years, work 2.3 (1.0 SD), economic 2.7 (1.2 SD). 2 years, work 2.3 (1.2 SD), economic 2.8 (1.3 SD). NPMD: Mean Life satisfaction at 7-8 years, work 2.1 (0.9 SD), economic 2.6 (1.2 SD). 4.5 years, work 2.2 (1.2 SD), economic 2.6 (1.4 SD). 2 years, work 2.5 (1.2 SD), economic 2.7 (1.4 SD). Paper reports no sig differences in any life satisfaction domains across diagnostic groups. BP: Mean Life satisfaction at 7-8 years, work 2.3 (1.0 SD), economic 2.5 (1.3 SD). 4.5 years, work 2.2 (1.1 SD), economic 3.0 (1.6 SD). 2 years, work 1.8 (1.1 SD), economic 3.0 (1.7 SD).	All time points Work: NPMD = PMD = BP Economic: PMD = NPMD = BP

Reference	Finding	Statistical comparisons
	Life satisfaction assessment: 1 = very satisfied, 5 = very dissatisfied.	
Sands[262] 1999 *Chicago Follow-up Study	PMD: Employment - FT 40%, PT/some 60%, none 0% (0/10). Activity (non- work) level – active 40%, marginal 50%, none 10% (1/10). SAD: Employment - FT 24%, PT/some 41%, none 35%. Activity (non-work) level – active 35%, marginal 47%, none 18%. NPMD: Employment - FT 56%, PT/some 27%, none 18% (6/34). Activity (non-work) level – active 71%, marginal 18%, none 12% (4/34). SZ: Employment - FT 14%, PT/some 20%, none 66%. Activity (non-work) level – active 36%, marginal 37%, none 37%.	Employment: NPMD = PMD Activity: NPMD = PMD Employment: PMD > SZ p<0.05 Activity: SZ = PMD Employment, none: NPMD > SAD p<0.05 Activity, none: SAD = NPMD Employment: SZ = SAD Activity: SZ = SAD Employment, none: SAD = PMD Activity, none: SAD = PMD
Tsuang[259] 1993	Mood congruent PMD: SCS: employment score – mean 2.7, S.D 1.7 Mood incongruent PMD: SCS: employment score – mean 2.9, S.D 1.6 SAD: SCS: employment score – mean 1.4, S.D 1.6 Schizophrenia: SCS: employment score – mean 1.1, S.D 1.4 Strauss carpenter (SCS): higher score indicates better adjustment.	Employment scores: Mood congruent & mood incongruent PMD groups > SZ p=0.0004 SZ = SAD Mood congruent PMD & Mood incongruent PMD > SAD p=0.02
Winokur[267] 1996 *DST 6 month study	PMD/SAD: Mean SADS occupational functioning in the past year (SD): 3.3 (3.4). Schizophrenia: Mean SADS occupational functioning in the past year (SD): 7.2 (3.2). Unstable diagnoses group: Mean SADS occupational functioning in the past year (SD): 3.8 (2.8). SADS occupational functioning: 1=no time out of work, 9=worked none due to psychopathology.	Occupational functioning: PMD/SAD > SZ (p=0.004) PMD/SAD > Unstable diagnoses group (p=0.0007)

< Means worse than; > means better than; = means equivalent outcomes

4.4.2.4.2. Relationship status

Only three papers reported on relationship status in PMD or SAD cases (Table 4-10). Only one of these papers compared PMD cases with schizophrenia cases. This paper reported that 61% of PMD cases were in a stable relationship at the end of a 15 year historical follow-up compared with 23% of schizophrenia cases (p=0.002).[180] No studies compared SAD cases with schizophrenia cases, or PMD or SAD cases with bipolar cases.

Based on this very limited literature, it was hypothesized that PMD and SAD cases would have a higher proportion of cases who were in a relationship over follow-up compared with schizophrenia cases.

Table 4-10: Relationship status outcomes

Reference	Finding	Statistical comparisons
Coryell[347] 1987a *NIMH Collaborative Study for the Affective Disorders	PMD: 9% married at intake were divorced at follow-up. 56% had fair-very poor friendships at 2yrs. NPMD: 9% married at intake were divorced at follow-up. 46% had fair-very poor friendships at 2yrs.	Divorced: PMD = NPMD Friendships: NPMD > PMD p<0.05
Jager[180] 2005	PMD: 61.1% in stable relationship. NPMD: 66.7% in stable relationship. SZ: 23.4% in stable relationship.	Stable relationship: PMD = NPMD PMD > SZ p=0.002
McGlashan[241] 1987 *Chestnut Lodge	SAD: 64% ever married. N33 SAM: 42% ever married. N19 SABP: 56% ever married. N 16	Ever married: SAM = SAD SABP = SAD

< means worse than; > means better than; = means equivalent outcomes

4.4.2.4.3. Social contact

Nine papers reported on social contact (see Table 4-11). Four papers reported on PMD and schizophrenia cases. Two papers reported PMD cases to have better scores on social contacts compared with schizophrenia cases,[258, 259] but only one of these were

statistically significant,[258] the other found no statistical difference.[259] Craig et al.[348] reported PMD cases to have lower (and therefore worse) scores on social outcomes compared with schizophrenia cases (mean 2.34 (1.37 S.D.) versus 2.89 (1.42 S.D.)) but this comparison was not statistically tested. Sands et al.[262] reported that less PMD cases had adequate social functioning (40% versus 49%) but the same amount had impoverished functioning (20% versus 20%) but there were no significant difference between the groups. Four papers reported on SAD and schizophrenia cases. All four papers reported SAD had better social contact outcomes (frequency / quality / social functioning / social contact scores) compared with schizophrenia.[239, 258, 259, 262] Only one reported the differences to be statistically different,[258] the others reported no statistical difference.[239, 259, 262] Within this thesis, data was available on a type of social contact outcomes: close confidants. However, no study reported on close confidants in PMD and SAD cases. Therefore, based on the literature above, it was hypothesized that PMD and SAD cases would have a higher proportion of cases who have close confidants compared with schizophrenia cases.

While no papers examined social contacts in SAD and bipolar cases, two papers reported on social contacts in PMD and bipolar cases within the same sample. However, one of these only reported on satisfaction with social contacts.[223] The other paper by Craig et al.[349] reported PMD cases to have lower (and therefore worse) scores on social outcomes compared with bipolar cases (mean 2.34 (1.37 S.D.) versus 4.19 (1.39 S.D.)) but this comparison was not statistically tested. Based on this very limited literature, the differences between PMD and SAD cases and bipolar cases in terms of social contacts is unclear.

Table 4-11: Social contact outcomes

Reference	Finding	Statistical comparisons
Craig[350] 1997 *Suffolk county	PMD (n42): social mean 2.34 (1.37 SD). BP (n64): social mean 4.19 (1.39 SD). SZ (n96): social mean 2.89 (1.42 SD). All p<0.001 but unclear between which diagnoses. Quality of life scale: 0 = worse functioning, 6 = best functioning.	Unclear
Maj[199] 1990 *Naples overlapping samples	PMD mood congruent: Mean DAS; social withdrawal 0.4 (0.6 SD); social contacts 0.7 (0.5 SD). NPMD: Mean DAS; social withdrawal 0.4 (0.4 SD); social contacts 0.6 (0.6 SD) DAS: higher scores indicate higher levels of disability.	No statistical comparisons
Brockington[351] 1982	RDC PMD: 33.9 mean social involvement score. SAD: 47.9 mean social involvement score. Social: higher scores indicate poorer adjustment.	Social involvement: PMD > SAD p<0.01
Coryell[236] 1988	SAD: 48.3% impaired social functioning. SABP: 14.3% impaired social functioning.	Impaired social functioning: SABP > SAD p<0.05
Sands[262] 1999 *Chicago Follow-up Study	PMD: Social functioning – adequate 40%, restricted 40%, impoverished 20%. SAD: Social functioning – adequate 59%, restricted 24%, impoverished 18%. NPMD: Social functioning – adequate 56%, restricted 24%, impoverished 21% SZ: Social functioning – adequate 49%, restricted 31%, impoverished 20%. No significant differences in social functioning	Social functioning: PMD = NPMD = SAD = SZ
Goldberg[223] 2005 *Chicago Follow-up Study	PMD: Mean Life satisfaction at 7-8 years, social 2.6 (1.4 SD). 4.5 years, social 2.4 (1.3 SD). 2 years, social 2.8 (1.4 SD). NPMD: Mean Life satisfaction at 7-8 years, social 2.7 (1.3 SD). 4.5 years, social 2.8 (1.2 SD). 2 years, social 2.7 (1.3 SD). BP: Mean Life satisfaction at 7-8 years, social 2.7 (1.2 SD). 4.5 years, social 2.9 (1.3 SD). 2 years, social 2.9 (1.4 SD). No sig differences in any life satisfaction domains across diagnostic groups.	All time points: Social: NPMD = PMD =BP Living: PMD = NPMD = BP

Reference	Finding	Statistical comparisons
	Life satisfaction assessment: 1 = very satisfied, 5 = very dissatisfied.	
Kendler[239] 1995	SAD: Mean (SD) Levels of functioning scale – Frequency of social contacts 2.8 (1.3), quality of social relations 2.3 (1.1). Affective illness: Mean (SD) Levels of functioning scale –Frequency of social contacts 4.2 (1.3), quality of social relations 3.7 (1.2). SABP: Mean (SD) Levels of functioning scale – Frequency of social contacts 3.5 (1.6), quality of social relations 3.0 (1.5). SZ: Mean (SD) Levels of functioning scale – Frequency of social contacts 2.2 (1.4), quality of social relations 1.6 (0.8). Levels of functioning: higher score indicates better adjustment.	SAD not statistically compared with affective illness or schizophrenia Social contacts: SAD = SABP Quality of social relations: SAD = SABP Ability to meet own needs: SAD > SABP $p<0.05$
Opjordsmoen[258] 1989	PMD: mean social contact score 2.5 (1.4). SAD: mean social contact score 1.7 (1.6). SZ: mean social contact score 0.8 (1.3). Social scores: higher score indicates better adjustment.	Social contacts: PMD > SZ $p<0.001$ SAD > SZ $p<0.01$ PMD > SAD $p<0.05$
Tsuang[259] 1993	Mood congruent PMD: SCS: social contacts score – mean 2.6, S.D 1.3 Mood incongruent PMD: SCS: social contacts score – mean 2.7, S.D 1.6 SAD: SCS: social contacts score – mean 2.5, S.D 1.3 Schizophrenia: SCS: social contacts score – mean 2.3, S.D 1.4 Strauss carpenter (SCS): higher score indicates better adjustment.	Social contacts: Mood congruent & mood incongruent PMD groups = SZ SZ = SAD SAD = Mood congruent PMD = Mood incongruent PMD

4.4.2.4.4. Prison

No papers reported on outcomes involving prison with PMD or SAD cases. However, in line with the findings reported above that PMD cases seem to have better psychosocial outcomes in other areas, it was hypothesized that PMD and SAD cases would have a lower proportion of cases who had been to prison compared with schizophrenia cases.

4.4.2.5. Service use

Of the 103 papers identified for this review, 35 of them had data on service use. Of these, 27 were on PMD, 4 were on SAD, 3 were on PMD and SAD and 1 was on PMD/SAD mixed. The papers on service use were focused mainly on inpatient service use (readmissions, time as an inpatient, continuously hospitalised etc) but there were also a number of papers which reported on other outcomes: outpatient events (mean time with service, proportion of groups using service); emergency room use; treatment (ECT, medication); follow-up service use status; and course of service use (e.g. one contact with services, continuous contact with services). However, the majority (28 out of 35) of the papers examined inpatient use. The finding that inpatient usage is the most researched area of service use is likely to be a reflection of the fact that inpatient use is generally the biggest cost driver.[352] Due to the dominance of literature on inpatient use, only inpatient use will be examined in this review.

4.4.2.5.1. Inpatient service use

Twenty-eight papers reported on inpatient service use. Nine of these papers reported on PMD and schizophrenia cases. Six of the nine papers report that PMD cases had better inpatient outcomes compared with schizophrenia cases (less rehospitalisations, lower scores on hospital outcomes, continuous hospitalisations).[180, 227, 229, 259, 262, 353] However, three papers report PMD cases to have worse inpatient outcomes compared with schizophrenia cases (more cases admitted, more hospitalisations).[1, 258, 354]

Four papers examined SAD and schizophrenia cases in the same study. Three reported that the inpatient outcomes were better in SAD cases (in terms of less hospitalisations, lower hospitalisation scores and less time in hospital)[259, 262, 355] compared with schizophrenia cases (although two of these comparisons were not statistically

significant[259, 262] and the other was not tested[356]). Only one study reported that SAD cases had better outcomes compared with schizophrenia cases. This was a 3-39 year follow-up of first admission patients by Opjordsmoen et al.[258] They reported that 3.4 mean hospitalisations (1.0 S.D.) in SAD cases compared with 2.4 in schizophrenia cases (1.5 S.D.; $p<0.05$). This literature shows a slight trend towards SAD having better inpatient outcomes.

Four studies reported on PMD and bipolar cases within the same study with very mixed results. One paper by Bromet et al.[227] reported PMD cases to have worse inpatient outcomes with 20.5 % of PMD cases being rehospitalised or never discharged in a six month follow-up compared with 17.7 % of bipolar cases being rehospitalised or never discharged. This result was not statistically significant. In a 6 month follow-up, Craig et al.[357] reported mixed results with less PMD cases being continuously hospitalised (0% versus 2%; not statistically tested) but more PMD cases being rehospitalised (20.5% versus 17.7%; not statistically different) compared with bipolar cases. A related paper by Craig et al.[229] based on the same sample reported on a two year follow-up and reported less PMD were rehospitalised compared with bipolar cases (29% versus 33%). A further paper by Winokur et al.[358] reported PMD cases to have less average hospitalisations compared with bipolar cases (3 versus 4) although this was not statistically significant. Only one paper reported on SAD and bipolar. Angst et al.[359] reported that 73% of SAD episodes involved hospitalisations but this was compared with a non-psychotic bipolar disorder group who had 56% of episodes involving hospitalisations.

Based on this literature it was hypothesized that PMD and SAD cases would have better service use outcomes compared with schizophrenia cases. In this thesis the service use

outcomes were proportion of cases admitted, number of hospitalisations, days hospitalised, percentage of the follow-up spent as an inpatient, percentage of compulsory admissions, proportion of cases being compulsorily admitted and percentage of hospitalisations involving the police. Therefore, the specific hypothesises were that PMD and SAD cases would have: a lower proportion of cases admitted; less hospitalisations; less days hospitalised; a lower percentage of the follow-up spent as an inpatient; a lower percentage of compulsory admissions; a lower proportion of cases being compulsorily admitted; and a lower percentage of hospitalisations involving the police, all compared with schizophrenia.

Table 4-12: Inpatient Service Use

Reference	Finding	Comparisons
Pederson[360] 1972	PMD: 86% of the original sample were hospitalised.	No comparison group
Miller[208] 1988 *Miller papers	PMD: 143 hospitalisations.	No comparison group
Brockington[361] 1980	SAD: mean 20.3% time in hospital. (+/- 15.2, n75) SZ: mean 36% time in hospital. (missing s.d., 53) PMD & PBP: mean 17% time in hospital. (missing s.d., n66)	No statistics in the paper and not enough information to conduct statistics.
Craig[229] 2000 *Suffolk county	PMD: 22/75 (29%) rehospitalised. Sz/SA: 83/155 (54%) rehospitalised. PBP: 39/119 (33%) rehospitalised.	No statistical tests
Crebbin[1] 2008	PMD: 81/105 (77%) patients admitted. SZ: 47/73 (64%) patients admitted.	No statistical tests
Kessing[181] 2003	PMD: 57.3% (731/1275) were readmitted. Severe depression without psychotic symptoms: 54.2% (888/1639) were readmitted. Mild/moderate depression without melancholia: 48.5% (142/293) were readmitted. Mild/moderate depression with melancholia: 49.2% (122/248) were readmitted.	No tests
Stephens[362] 1982	PMD: time in hospital in follow-up mean 0.5 (0.7 SD), months hospitalises mean 6.6 (5.1 SD). SZ: time in hospital in follow-up mean 1.6 (1.6 SD), months hospitalises mean 5.1 (4.2 SD). SA: time in hospital in follow-up mean 1.3 (1.4 SD), months hospitalises mean 6.0 (6.8 SD). Unspecified psychosis: time in hospital in follow-up mean 0.8 (1.1 SD), months hospitalises mean 5.2 (5.7 SD). Proportion of time hospitalised during follow-up: 1 = </= 10%, 2 = 11-25%, 3 = 26-74%, 4 = >/= 75%.	Not individually compared
Angst[363] 1995a *Angst &	SAD: Episodes with hospitalisations = 73% (77/106) NPMD: Episodes with hospitalisations = 61% (84/137) NPBP: Episodes with hospitalisations = 56% (27/49)	No specific diagnoses compared

Reference	Finding	Comparisons
Preisig 1995 papers	SAM: Episodes with hospitalisations = 81% (92/114)	
Bromet[227] 1996 *Suffolk county	PMD: 20.5 % rehospitalised or never discharged. SZ: 24.5 % rehospitalised or never discharged. BP: 17.7 % rehospitalised or never discharged.	PMD = BP PMD = SZ
Charney[364] 1981	PMD: 2.54 (1.78) prior hospitalisations. NPMD: 2.17 (1.66) prior hospitalisations.	PMD = NPMD
Copeland[172] 1983	PMD: 1.5 mean readmissions due to depression, 0-2.5 years – mean 13 weeks as inpatient, total hospital surveillance 60 weeks, 2.5-5 years – mean 7 weeks an inpatient), total hospital surveillance 31 weeks. Hospital surveillance mean 91 weeks. Immediate outcome = 10 weeks in hospital. Neurotic depression: 0.2 mean readmissions due to depression, 0-2.5 years – mean 1.3 weeks as an inpatient, total hospital surveillance 16 weeks, 2.5-5 years - mean 0.3 weeks as an inpatient, total hospital surveillance 1.9 weeks. Hospital surveillance mean 18 weeks. Immediate outcome = 8 weeks in hospital.	Mean readmissions: NPMD > PMD p<0.02 2.5 year mean inpatient weeks: NPMD > PMD p<0.01 2.5 year hospital surveillance: NPMD > PMD P<0.001 5 year mean inpatient weeks: PMD = NPMD Total 5 year hospital surveillance: NPMD > PMD p<0.05 Mean hospital surveillance: NPMD > PMD P<0.01 Immediate outcome: PMD = NPMD
Coryell[365] 1986b *Coryell 86	PMD: - 16/46 (35%) rehospitalised NPMD: 43/159 (27%) rehospitalised	Rehospitalisation: PMD = NPMD p>0.05
Coryell[366] 1987a *NIMH collaborative depression study	PMD: Of the 46 hospitalised at intake, 26% (12/46) were rehospitalised only once, 9% (4/46) twice and 13% (6/46) more than twice. N46 NPMD: Of the 318 hospitalised at intake, 21% (67/318) were rehospitalised only once, 10% (32/318) twice and 11% (35/318) more than twice. N318	Rehospitalised once: PMD = NPMD Rehospitalised twice: NPMD = PMD Rehospitalised more than twice: PMD = NPMD
Craig[367] 1997 *Suffolk county	PMD: 0/42 (0%) continuously hospitalised. 20.5% rehospitalised. SZ: 4/96 (4%) continuously hospitalised. 23.4% rehospitalised. BP: 1/64 (2%) continuously hospitalised. 17.7% rehospitalised.	Continuously hospitalised: not tested

Reference	Finding	Comparisons
		Rehospitalised: PMD = BP PMD = SZ
Frances[368] 1981	PMD: 54.3 inpatient days required. NPMD: 39.8 inpatient days required.	Inpatient days: NPMD > PMD p=0.02
Jager[180] 2005	PMD: mean 2.8 rehospitalisations. NPMD: mean 1.3 rehospitalisations. SZ: mean 2.9 rehospitalisations.	Rehospitalisations SZ = PMD NPMD > PMD p=0.045
Johnson[73] 1991	PMD: 0 new hospitalisations, 10.9% medical hospitalisations. NPMD: 1.5% new hospitalisations, 11.4% medical hospitalisations.	new hospitalisations: NPMD = PMD medical hospitalisations: NPMD = PMD
Lykouras[184] 1994	PMD: mean 1.75 (0.91) hospitalisations. NPMD: mean 1.32 (0.62) hospitalisations.	PMD = NPMD
Maj[185] 2007	PMD: Retrospective: 3.9 mean prior hospitalisations. NPMD: Retrospective: 2.7 mean prior hospitalisations. Depression with preoccupations: Retrospective: 3.3 mean prior hospitalisations.	Hospitalisations: NPMD > PMD p<0.0001 Depression with preoccupations > PMD p<0.03
Parker[369] 1991	PMD: 91% (32/35) were admitted. NPMD: 66% (23/35) were admitted. PMD: 48% (17/35) were readmitted. NPMD: 26% (9/35) were readmitted.	Admitted: NPMD > PMD p=0.004 Readmitted: not tested
Robinson[189] 1985	PMD: patients hospitalised 11/52, total number of hospitalisations 18. NPMD: patients hospitalised 7/52, total number of hospitalisations 10.	Hospitalised: PMD = NPMD Hospitalisations: PMD = NPMD
Winokur[370] 1985 *Angst 86?	PMD: 3 hospitalisations NPMD: 2 hospitalisations PBP: 4 hospitalisations NPBP: 2 hospitalisations	PMD = NPMD PMD vs. PBP vs. NPBP not tested
Maj[242] 1985 *Naples overlapping samples	SAD: RETROSPECTIVE - mean hospitalisations 1.8 mean (1.3). PROSPECTIVE –0.6 (0.7) mean hospitalisations, 0.8 (0.9) mean months in hospital. SAM: RETROSPECTIVE - mean hospitalisations 1.8 mean (1.4). PROSPECTIVE – 0.4 (0.6) mean hospitalisations, 0.4 (0.5) mean months in hospital. Non-psychotic Mania: RETROSPECTIVE - mean hospitalisations 1.9 mean (0.9). PROSPECTIVE –0.4 (0.6) mean hospitalisations, 0.3 (0.4) mean months in hospital. NPMD: RETROSPECTIVE - mean hospitalisations 2.2 mean (1.0). PROSPECTIVE –0.5 (0.6) mean hospitalisations, 0.5 (0.9) mean months in hospital.	Retrospective: Hospitalisations: NPMD = SAD Prospective: hospitalisations: SAD = NPMD Months in hospital: SAD = NPMD SAD not compared with SAM or NPmania
McGlashan[241] 1987 *Chestnut	SAD: Length of stay at Chestnut Lodge 39 months SAM: Length of stay at Chestnut Lodge 37 months SABP: Length of stay at Chestnut Lodge 69 months	Length of stay: SAD = SABP SAD = SAM

Reference	Finding	Comparisons
Lodge		
Tsuang[259] 1993	Mood congruent PMD: SCS: Hospitalisation score - mean 3.3, S.D 1.3 n17 Mood incongruent PMD: SCS: Hospitalisation score - mean 3.3, S.D 1.4 n 15 SAD: SCS: Hospitalisation score - mean 3.0, S.D 1.2 n 11 Schizophrenia: SCS: Hospitalisation score - mean 2.7, S.D 1.5 n22 Strauss carpenter (SCS): higher score indicates better adjustment.	Hospitalisation score: SZ = SAD = Mood congruent PMD = mood incongruent PMD
Opjordsmoen[258] 1989	SAD: Mean hospitalisations 3.4 (1.0), PMD: Mean hospitalisations 3.8 (0.5), SZ: Mean hospitalisations 2.4 (1.5),	Mean hospitalisations: SAD > PMD $p < 0.05$ SZ > PMD $p < 0.05$ SZ > SAD $p < 0.05$
Sands[262] 1999 *Chicago Follow-up Study	PMD: Rehospitalisations – None 90%, Less than 3 months 10%, 3 months + 0%. SAD: Rehospitalisations – None 76%, Less than 3 months 29%, 3 months + 0%. SZ: Rehospitalisations – None 49%, Less than 3 months 40%, 3 months + 11%. NPMD: Rehospitalisations – None 73%, Less than 3 months 27%, 3 months + 0%.	Rehospitalisations: PMD = SAD PMD = SZ PMD = NPMD SAD = SZ SAD = NPMD
Brockington[371] 1982	RDC PMD: 16.8% mean time spent in hospital. SAD: 10.0% mean time spent in hospital. DSM PMD Mood congruent: 15.3% mean time spent in hospital. PMD Mood incongruent: 11.4% mean time spent in hospital. NPMD: 17.1% mean time spent in hospital. Catego: PMD: 15/16 (94%) readmitted. Neurotic depression: 9/20 (45%) readmitted. Retarded depression: 8/18 (44%) readmitted.	RDC – time in hospital: PMD = SAD DSM – time in hospital: PMD congruent & PMD incongruent > NPMD $p<0.01$ Catego – readmitted: neurotic depression & retarded depression > PMD $p<0.01$

< Means worse than; > means better than; = means equivalent outcomes

4.5. Discussion

4.5.1. Summary of the findings

There are several key points to take from this review:

1. There is very little research on SAD.
2. Much of the research is contradictory which is likely due to the substantial differences in methodologies.
3. There are only four studies based on the best sampling method – incidence samples.

Based on these key points, an incidence study of long-term outcomes in PMD and SAD cases compared with schizophrenia and bipolar cases is needed to advance the literature.

4.5.2. Methodological limitations in the literature

This review highlights a number of key methodological limitations within the literature. There are few studies examining outcomes in PMD and SAD cases that are based on the best source of evidence – incidence samples. Of the papers that do use these samples, they are over relatively short periods of time (6 months – 4 years); therefore, knowledge of long-term outcomes is limited.

Even the four studies which were based on first episode psychosis samples had some methodological flaws. Two of the papers did not report confidence intervals[78, 197] which, as discussed in section 5.5.10.3, is important in the interpretation of results. One paper also did not appear to match controls or control for differences between cases and controls in the analysis.[78]

A further issue with previous literature is that in many studies it is unclear whether the bipolar disorder group includes psychotic bipolar disorder, non-psychotic bipolar disorder, or both. This makes it difficult to tell who the PMD or SAD group is actually being compared with and could be the reason for inconsistent findings.

One issue that has not been addressed in this review so far is the issue of the influence of diagnostic change on other outcomes. Since diagnostic stability in PMD and SAD cases is relatively low, other outcomes may be influenced by this instability. For example, based on an initial diagnosis, PMD may have lower suicide attempt rates compared with schizophrenia. However, if a substantial proportion of PMD cases change to a different diagnosis, the results are likely to change. Therefore, accounting for diagnostic change is very important in examining outcomes.

4.5.3. Limitations of this review

This review is not without its limitations. Due to the heterogeneous nature of the studies, a meta-analysis was not possible; therefore a narrative review has been used to assimilate the data from the systematic searches. This is not ideal as narrative reviews often do not meet important criteria to help mitigate bias.[372] However, this is the first systematic review of the course and outcome of PMD and SAD and as such, is thought to be more reliable than selective literature reviews.

4.5.4. Implications for this thesis

Based on the literature and the methodological issues mentioned above, this thesis aimed to use an incidence psychosis sample of PMD and SAD cases, followed up over a

long (at least 8 years) period and based on both the baseline and lifetime diagnoses, to investigate the following outcomes:

1. Diagnostic stability including prospective and retrospective consistency;
2. Course of illness, namely, course type (episodic, continuous and neither), longest remissions, number of episodes, length of remissions and percentage of time psychotic;
3. Mortality and suicidality, namely, deaths from all causes, completed suicide, suicide attempts and self-harm;
4. Social outcomes, namely, employment status, relationship status, close confidants and time in prison;
5. Inpatient service use, namely, the proportion of hospitalisations, days hospitalised, percentage of follow-up as an inpatient; compulsory admissions; and admissions involving the police.

These outcomes were compared against outcomes for schizophrenia and psychotic bipolar disorder cases.

4.5.4.1. Hypotheses

The following were hypothesized based on the literature discussed above:

1. PMD and SAD cases will have a lower prospective consistency and higher retrospective consistency compared with schizophrenia and bipolar disorder cases.
2. PMD and SAD cases will have a higher proportion of cases with an episodic course of illness and less with a continuous course of illness compared with schizophrenia cases.

3. PMD and SAD will have: longer remissions; more episodes; shorter episodes; and will spend a smaller percentage of the follow-up psychotic, all compared with schizophrenia cases.
4. PMD and SAD cases will have a higher proportion of cases who die (from all causes) over the follow-up compared with schizophrenia and bipolar cases.
5. PMD and SAD cases will have a higher proportion of cases who complete suicide over the follow-up compared with schizophrenia and bipolar cases.
6. PMD and SAD cases will have a higher proportion of cases who attempt suicide over the follow-up, and a higher rate of suicide attempts for those who do attempt, compared with schizophrenia and bipolar cases.
7. PMD and SAD cases will have a higher proportion of cases who self-harm over the follow-up, and a higher rate of self-harm events for those who do self-harm, compared with schizophrenia and bipolar cases.
8. In terms of social outcomes over follow-up, PMD and SAD cases will have a higher proportion of cases who are: employed; in a relationship; have close confidants; and a lower proportion of cases who have been to prison, all compared with schizophrenia cases.
9. In terms of service use, PMD and SAD cases will have: a lower proportion of cases admitted; less hospitalisations; less days hospitalised; a lower percentage of the follow-up spent as an inpatient; a lower percentage of compulsory admissions; a lower proportion of cases being compulsorily admitted; and a lower percentage of hospitalisations involving the police, all compared with schizophrenia.

CHAPTER 5. Methodology

"If you torture your data long enough, they will tell you whatever you want to hear."[373]

Mills (1993)

5.1. Aims of the chapter

The aim of this chapter was to provide a full account of the methods used in this thesis. This will include specifying the aims and hypotheses of the study, describing the full procedure used in this thesis and giving a background to the ÆSOP study, the study from which data used in this thesis were drawn.

5.2. Aims of the study

As discussed in chapter 3 and chapter 4, this PhD thesis had three main aims:

1. To examine the role of psychosocial risk factors in PMD and SAD cases, within a study that overcomes the three major methodological limitations of previous research (separating PMD and SAD cases from other diagnoses, sampling from an incidence psychosis sample, and accounting for diagnostic stability).
2. To investigate the long-term diagnostic stability, course of illness, mortality and suicidality, social and inpatient service use outcomes for PMD and SAD cases, while overcoming major limitations from previous research (by sampling from incidence psychosis samples).
3. To compare the above between cases with PMD and SAD to the other major psychotic diagnostic groups of schizophrenia and bipolar disorder with psychotic features.

5.3. Outline

This thesis is based on data from the Aetiology and Ethnicity in Schizophrenia and Other Psychoses (ÆSOP) study. The ÆSOP study is made up of 2 parts: an epidemiological, case-control study of the incidence of psychosis (also referred to as baseline); and a cohort follow-up study (also referred to as follow-up; see figure 5-1).

The data from both of these sections of the study are used within this thesis. The study methodology will be presented in two sections: case control and cohort.

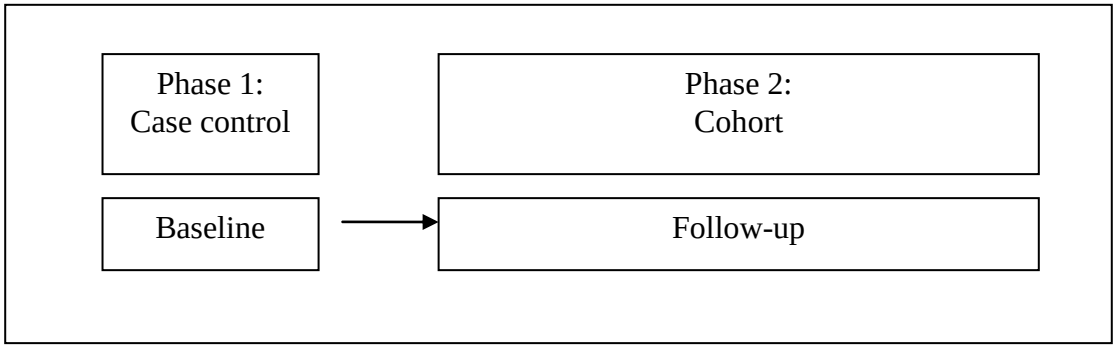


Figure 5-1: Outline of study

The ÆSOP study has been documented previously.[374-382]

5.4. Background to the ÆSOP study

This section aims to describe some background information about the recruitment locations, specifically: employment and income deprivation; population density; and ethnic density.

The ÆSOP study was based in 3 tightly defined areas in the UK; South-east London; Nottingham; and Bristol (see Figure 5-2). The south-east London site had an inclusion area which covered the local authority boroughs of Lambeth and two-thirds of Southwark. This inclusion area was a portion of the Maudsley, South Western and St. Thomas' hospitals catchment area within the former Bethlem and Maudsley NHS trust. The Nottingham site inclusion areas included the local authority boroughs of Ashfield, Broxtowe, Gedling, Rushcliffe and Nottingham. This inclusion area consisted of part of the Nottingham Healthcare NHS Trust catchment area. The Bristol site inclusion area was the Bristol local authority alone, which made up one of the seven local authorities covered by the Avon and Wiltshire Mental Health Partnership NHS trust catchment

area. Due to financial restraints, Bristol case control cases were not followed up and were consequently excluded from this thesis. Therefore, only information on the London and Nottingham sites will be described from henceforth.

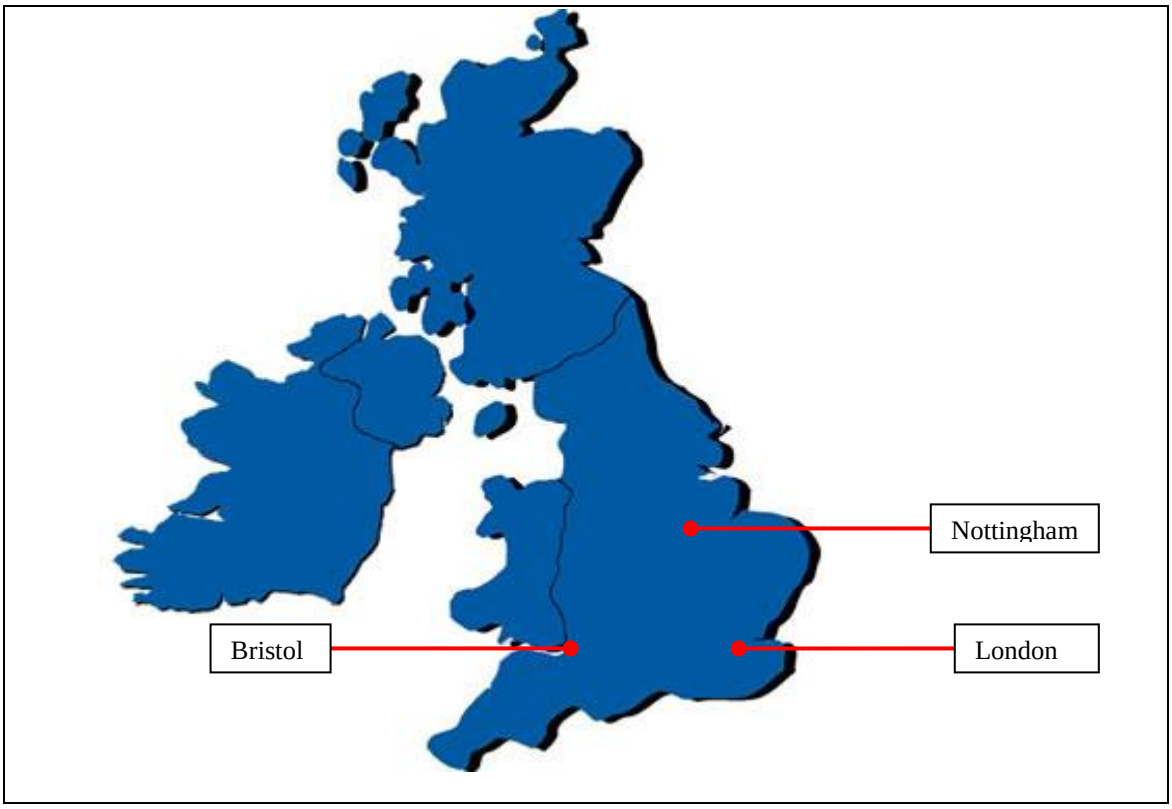


Figure 5-2: Map of recruitment sites

5.4.1. Employment and Income Deprivation

The employment deprivation and income deprivation ranks published in 2000 (around the time of the case control study) for both the London and Nottingham sites are reported in Table 5-1. The ranks are reported for each local authority in England and are therefore out of a total of 354. A lower rank indicated greater level of employment deprivation and income deprivation such that a rank of 1 signifies the most employment and income deprived and a rank of 354 signifies the least employment and income deprived. The two inner-city boroughs covered by the London site had a median rank employment deprivation score of 19.5 out of 354 local authorities across England (range

17-22).[383] The median rank income deprivation score was 22 out of 354 (range 21-23).[383] The five boroughs covered by the Nottingham site had a median rank employment deprivation score of 128.5 out of 354 local authorities across England (range 14-243).[383] The median rank income deprivation score was 146.5 out of 354 (range 10-283).[383] The ranges of the employment and income deprivation scores in Nottingham vary dramatically highlighting the differences even within this one site.

Table 5-1: Employment Deprivation and Income Deprivation 2000

Site	Local Authority	Employment Deprivation Rank	Income Deprivation Rank
London	Lambeth	17	21
	Southwark	22	23
Nottingham	Ashfield	106	112
	Broxtowe	177	118
	Gedling	163	178
	Rushcliffe	243	283
	Nottingham	14	10

Information taken from Department of the Environment, Transport and the Region 2000 [383].

The employment deprivation and income deprivation ranks published in 2007 (around the time of the follow-up of the cohort study) for the London and Nottingham sites are reported in Table 5-2.

Table 5-2: Employment Deprivation and Income Deprivation 2007

Site	Local Authority	Employment Deprivation Rank	Income Deprivation Rank
London	Lambeth	16	16
	Southwark	22	18
Nottingham	Ashfield	111	124
	Broxtowe	183	217
	Gedling	175	194
	Rushcliffe	281	298
	Nottingham	12	13

Information taken from The English Indices of Deprivation by Noble and Colleagues, 2007

The two inner-city boroughs covered by the London site had a median rank employment deprivation score of 19 out of 354 local authorities across England (range 16-22).[384] The median rank income deprivation score was 17 out of 354 (range 16-18).[384]

The five boroughs covered by the Nottingham site had a median rank employment deprivation score of 146.5 out of 354 local authorities across England (range 12-281).[384] The median rank income deprivation score was 155.5 out of 354 (range 13-298).[384] Again, the ranges of the employment and income deprivation scores in Nottingham vary dramatically highlighting the differences even within this one site.

5.4.2. Population Density

Table 5-3 shows the population density for the London and Nottingham sites in 2002 (between the case control and follow-up for the cohort study). The Median population density for London was 9,423 (range 8,710-10,136).[385] The Median population density for Nottingham was 1,939 (range 259-3,619).

Due to its high population density, participants from the London site were considered as coming from a high population density environment. Nottingham having a lower population density was therefore considered a low population density environment.

Table 5-3: Population Density 2002

Site	Local Authority	People per square kilometre
London	Lambeth	10,136
	Southwark	8,710
Nottingham	Ashfield	1,043
	Broxtowe	1,345
	Gedling	933
	Rushcliffe	259
	Nottingham	3,619

Information taken from The Office of National Statistics, 2002[385]

5.4.3. Ethnic Density

Table 5-4 shows the ethnic composition of the populations from each site by local authority in 2001 (between the case control and follow-up phase of the cohort study). The figures highlight the relatively low proportions of non-White British ethnic groups

in Nottingham (81.0-93.9% White British inhabitants)[386-390] compared with the London site (50.0-52.3% White British Inhabitants).[391, 392]

Table 5-4: Ethnic Composition 2001

Site	Local Authority	Ethnicity percentage	
London	Lambeth[391]	White British 50.0	Other Asian 0.8
		White Other 12.8	Black Caribbean 11.9
		Mixed 4.8	Black African 11.4
		Indian 2.0	Black Other 2.1
		Pakistani 1.0	Chinese 1.3
		Bangladeshi 0.8	Other Ethnic Group 1.2
	Southwark[392]	White British 52.3	Other Asian 0.6
		White Other 10.9	Black Caribbean 7.9
		Mixed 3.7	Black African 15.9
		Indian 1.5	Black Other 1.8
		Pakistani 0.5	Chinese 1.9
		Bangladeshi 1.5	Other Ethnic Group 1.5
Nottingham	Ashfield[387]	White British 98.0	Other Asian 0.0
		White Other 0.9	Black Caribbean 0.1
		Mixed 0.4	Black African 0.0
		Indian 0.2	Black Other 0.0
		Pakistani 0.1	Chinese 0.1
		Bangladeshi 0.0	Other Ethnic Group 0.1
	Broxtowe[388]	White British 87.7	Other Asian 0.4
		White Other 3.6	Black Caribbean 0.6
		Mixed 1.5	Black African 0.6
		Indian 2.0	Black Other 0.1
		Pakistani 0.8	Chinese 1.7
		Bangladeshi 0.3	Other Ethnic Group 0.8
	Gedling[389]	White British 93.9	Other Asian 0.1
		White Other 2.3	Black Caribbean 0.8
		Mixed 1.0	Black African 0.1
		Indian 0.8	Black Other 0.1
		Pakistani 0.4	Chinese 0.3
		Bangladeshi 0.0	Other Ethnic Group 0.1
	Rushcliffe[390]	White British 93.2	Other Asian 0.1
		White Other 2.8	Black Caribbean 0.3
		Mixed 1.1	Black African 0.1
		Indian 1.4	Black Other 0.0
		Pakistani 0.5	Chinese 0.3
		Bangladeshi 0.0	Other Ethnic Group 0.2
	Nottingham[386]	White British 81.0	Other Asian 0.4
		White Other 3.9	Black Caribbean 3.4
		Mixed 3.1	Black African 0.5
		Indian 2.3	Black Other 0.4
		Pakistani 3.7	Chinese 0.6
		Bangladeshi 0.2	Other Ethnic Group 0.5

Information taken from the Office of National Statistics, 2001

This background section has highlighted the differences in employment deprivation, income deprivation, population density and ethnic density between the three recruitment sites. It is clear that London has very high deprivation levels compared with

Nottingham, London has high population density compared with Nottingham, and London has a much higher proportion of non-white British inhabitants compared with Nottingham. However, it also highlights the variation within each site with Nottingham having large variation of all of the social context factors examined.

5.5. Phase 1 – case control study

The case control phase of the study was used to investigate the psychosocial risk factors associated with a diagnosis of PMD and SAD, and to test the hypotheses outlined at the end of Chapter 3.

5.5.1. Design

The case control study recruitment occurred in two stages:

1. An incidence study which aimed to count the number of psychosis cases and collate sociodemographic and clinical data from case notes.
2. A case control study which aimed to recruit, consent and interview as many of the incidence cases as possible.

5.5.2. Participants

5.5.2.1. Cases

Within the specified geographical areas, all cases with a first episode of psychosis (codes F20–29 and F30–33 in ICD–10[14]) who presented to secondary services (i.e. inpatient units, outpatient units, community mental health teams, assertive outreach teams, emergency clinics and private sector clinics) were included in the incidence study. Table 5-5 gives details on the diagnoses included. For the purpose of this thesis,

cases with bipolar disorder and mania will be included into the same diagnostic group and referred to as bipolar disorder cases.

Table 5-5: All diagnoses included in the ÆSOP study

Code	Diagnosis	Subtypes
F20	Schizophrenia	Paranoid, Hebephrenic, Catatonic, Undifferentiated
F21	Schizotypal Disorder	
F22	Persistent Delusional Disorder	Delusional disorder, other persistent delusional disorders
F23	Acute and Transient Psychotic Disorder	Acute psychotic disorder without schizophrenic symptoms Acute psychotic disorder with schizophrenic symptoms Acute schizophrenia-like psychotic disorder Other acute delusional psychotic disorder Other acute transient psychotic disorder
F24	Induced Delusional Disorder	
F25	Schizoaffective Disorder	Manic type, Depressive type, Mixed type, Unspecified
F28	Other Nonorganic Psychotic Disorder	
F29	Unspecified Nonorganic Psychosis	
F30	Mania Episode	Mania with psychotic symptoms
F31	Bipolar Affective Disorder	Current episode manic with psychotic symptoms Current episode depressed, severe with psychotic symptoms
F32	Depressive Episode	Severe depressive episode with psychotic symptoms
F33	Recurrent Depressive Disorder	Current episode severe with psychotic symptoms

Information from the ICD-10[14]

Cases who presented to these services were screened for eligibility using the Screening Schedule for Psychosis[393] (Appendix C). The Screening Schedule for Psychosis is a checklist which identifies both positive and negative symptoms of psychosis in a participant. The Screening Schedule for Psychosis was completed using information from clinical notes and corroboration from mental health staff, or where possible, by interview with the participant. Every person who was screened and found to be positive for psychosis was included in the incidence study and then invited to participate in the case control section of the study. Participants were given an information sheet

(Appendix D) which they read and had explained to them. Once the case understood the study, they were asked to give written consent (Appendix E).

Exclusion criteria for the study were:

- Aged less than 16 years or over 65 years.
- Had evidence of psychotic symptoms precipitated by an organic cause.
- Had transient psychotic symptoms resulting from acute intoxication as defined by ICD– 10.[14]
- Had previous contacts with mental health services for psychosis.
- Had moderate or severe learning difficulties or an IQ of less than 50.[14]

5.5.2.2. Controls

The ÆSOP study also collected data from a sample of non-psychotic controls. This was done using a population-based selection approach. Population-based selection approaches have advantages over facility-based selection and family-based selection which "...assume that patients with the disease of the cases originate in the same source population as patients admitted with the disease of the controls. This assumption is not always realistic".[160] Population-based selection is preferred as "...the cases are representative of all people with new onset of the disorder (incident cases) in a defined population over a specified time period...".[160] However, there is an assumption that controls developing the same diseases as cases would present to the same services. Bromet et al. highlight that "such assumptions are difficult to verify".[160] The impact of this is discussed further in chapter 8.

Control participants were recruited using the postal address file (PAF) method described by Jenkins and Meltzer.[394] The PAF was used to generate a random sample of 10 target

addresses that was within the same postcode as each of the psychosis cases. This ensured matching of cases and controls in terms of geographic location. The first of the target addresses was visited by researchers on three separate occasions, at different times of day (morning, afternoon and evening) and on different days to ensure maximum likelihood of contact being made and to minimise the sampling bias of unemployed people being more likely to be at home during the day. If there were no responses from the address or if there was a refusal from occupants then the next target address was approached.

An eligible resident was sought from each address. Written informed consent was sought from each control (Appendix F). A Kish[395] grid was used to randomly select one control if more than one eligible control was selected from each household. A Kish grid is a list of predefined numbers which are used to select a potential participant. All potential participants from the same address were listed in age order and then the participant corresponding with the Kish grid number were selected for interview.[395] This allowed all potential participants within a household to have an equal chance of selection.

Exclusion criteria for the study were:

- Had previous contacts with mental health services for psychosis.
- Aged less than 16 years or over 65 years.
- Had an insufficient level of English to complete the interviews.
- Had moderate or severe learning difficulties or an IQ of less than 50.[14]

Once a control had given written informed consent, they were asked to complete the Psychosis Screening Questionnaire (PSQ).[396] The PSQ (Appendix G) developed by

Bebbington and Nayani is a schedule designed to screen for psychotic symptoms in the general population and is usable by lay interviewers. If a potential control screened positive on the PSQ, a SCAN (see section 5.5.6.2) interview was completed, and anyone with a psychotic disorder was excluded. Control participants were not excluded if they had experienced or were currently experiencing any mental illness or symptoms of mental illness other than psychosis.

5.5.3. Timelines

Recruitment occurred over a 3-year period. From 1st September 1997 to the 31st August 1999 all eligible participants were approached for recruitment into the study. From 1st September 1999 to 31st August 2000 participants of a Black Caribbean ethnic origin were recruited in order to increase the power for a case-control analysis (see Figure 5-3). Only cases from the 2 year incidence sample plus the leakage cases (discussed in section 5.5.4) were used in this PhD thesis as the aim was to explore the risk factors and outcomes in an epidemiological first episode sample.

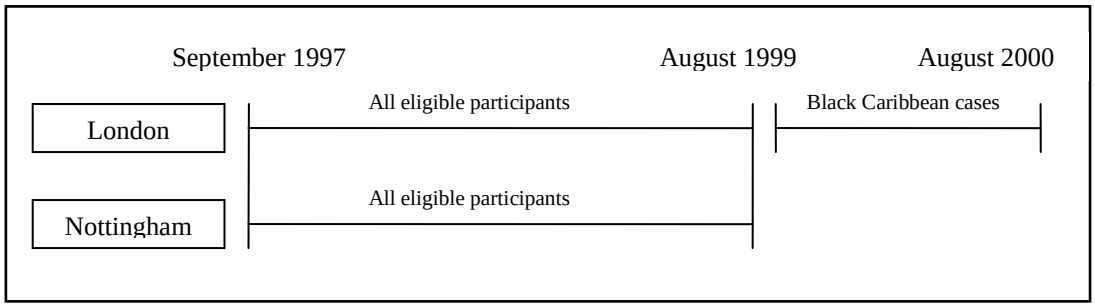


Figure 5-3: Recruitment by site

5.5.4. Leakage study

At the end of the recruitment period a leakage study was performed to identify any eligible participants who had been missed by the main recruitment method. The leakage

methodology described by Cooper and colleagues [397] was used to identify further participants who were missed. This involved checking with local private psychiatric hospitals and local private practising psychiatrist as well as checking the relevant psychiatric registers. These participants were included in the incidence section of the study but were not approached to be recruited into the case control study. As for all incidence cases, case notes were used to gain sociodemographic and clinical data.

5.5.5. Data collection

Cases for the incidence study were identified by members of the research team regularly checking all points of contact with mental health services within the catchment areas. Case notes were then accessed to compile information about sociodemographics and clinical picture.

Cases who consented to participate in the case control study were asked to complete a battery of schedules over an average of 4 interviews. The assessments took an average of 6 hours to complete. Participants were also asked for their permission for the team to interview a relative with whom they had recent contact with for the purpose of corroborating information.

5.5.6. Measures

The literature review in Chapter 3 drew out key psychosocial factors to investigate in this thesis. These were age, gender, ethnicity, place of birth, employment, education, social isolation, life events and childhood adversity. Within this thesis, social isolation was indicated using a number of proxy variables. These were relationship status, living circumstances, contact with friends, contact with family and close confidants. Data on

these were collected using the Medical Research Council Socio-demographic Schedule.[398]

Although a battery of schedules was conducted with each of the participants and controls for the larger AESOP study, only a small number of them were relevant for this thesis. Table 5-6 shows the schedules that were used in this thesis and the source of information for each schedule. These were the Medical Research Council Socio-demographic Schedule (MRC-SDS),[398] the Schedules for Clinical Assessment in Neuropsychiatry (SCAN),[399] the Personal and Psychiatric History Schedule (PPHS),[400] the Childhood Experiences of Care and Abuse Questionnaire (CECA-Q)[401] and the Life Events and Difficulties Schedule (LEDS).[402, 403] Previous research has validated the CECA-Q[404, 405] and LEDS.[36]

Table 5-6: Baseline assessments

Type of data	Schedule	Source of data
Clinical	Schedules for Clinical Assessment in Neuropsychiatry (SCAN)[399]	Patient Case notes Staff informant Relative
	Personal and Psychiatric History Schedule (PPHS)[400]	Patient Case notes Staff informant Relative
Social	MRC Sociodemographic Schedule (MRC-SDS)[398]	Patient Case notes Staff informant Relative
Psychosocial	Childhood Experiences of Care and Abuse Questionnaire (CECA-Q)[401]	Patient Case notes
	Life Events and Difficulties Schedule (LEDS)[402, 403]	Patient Case notes
Biological	Family Interview for Genetics (FIGS)[406]	Patient Relative

Amended from Morgan et al., 2006[380]

5.5.6.1. Medical Research Council Socio-demographic Schedule

The Medical Research Council Socio-demographic Schedule (MRC-SDS)[398] was used to collect data on: centre; age; ethnicity; gender; highest educational level achieved; place of birth; current and historical employment status; current and living circumstances; and current and historical relationship status (Appendix H). For those participants who declined to be interviewed, the MRC-SDS was completed as far as possible using the patient's case notes.

Participants self-ascribed their own ethnicity from the Census categories.[407] For those participants who were not interviewed, place of birth and place of parent's birth was used to assign ethnicity by consensus within the team. The ethnic groups were then reorganised from the 9 original categories into 6 new categories: White British (previously White); African Caribbean (Black Caribbean and Black other); Black African; White Other (previously White); Asian (Indian, Pakistani and Bangladeshi) and Other (Chinese and other).

5.5.6.2. Schedules for Clinical Assessment in Neuropsychiatry

The Schedules for Clinical Assessment in Neuropsychiatry , Version 2 (SCAN, V2)[399] incorporates the Present State Examination Version 10, to determine whether a range of symptoms are present, and how severe they are. [408] These symptoms are part of a comprehensive and defined list. The SCAN was used to determine the present mental state at baseline, i.e. the one month around the time of first presentation. The SCAN is comprised of two sections. Part 1 examines non-psychotic symptoms and part 2 examines psychotic and cognitive disorders.[409] A shortened version of the SCAN was used to focus solely on symptoms of depression, mania and psychosis.

Where an interview with the patient was not possible, case notes, clinicians and other informants were used to gain information to complete the Item Group Checklist (IGC) section of the SCAN.[399]

5.5.6.3. Personal and Psychiatric History Schedule

The Personal and Psychiatric History Schedule (PPHS)[400] is a semi-structured interview about a patient's psychiatric history and the circumstances surrounding the patient's current episode (Appendix I). The PPHS was used for a number of purposes.

Firstly, it was used to gather clinical information about the first episode of illness and initial modes of treatment. The PPHS collates information on the details and circumstances of current outpatient treatment, details and circumstances of current inpatient treatment, reasons for current treatment and general psychiatry history. This provides a detailed psychiatric history.

Secondly, the PPHS was used to gather data on pathways to care and mode of contact with services. Pathways to care were defined as contacts initiated by or on behalf of the cases in the period immediately before their presentation to secondary mental health services with a first episode of psychosis. These contacts included NHS and Criminal Justice System contacts as well as alternative contacts such as traditional healers and church leaders. The PPHS section on pathways to care was extended to include two extra items. These were who initiated help-seeking and a space for a detailed narrative description of the pathway to care.

Finally, the PPHS was used to collect information on the duration of untreated psychosis. Duration of untreated psychosis was defined very similarly to that described

by Craig and colleagues as the period from onset to the point of contact with secondary mental health services (i.e. receipt of either an inpatient admission or treatment in/contact with an outpatient facility for a psychotic disorder).[410] Onset was defined in line with previous research as the presence for one week or more of: delusions; hallucinations; formal thought disorder; marked psychomotor disorder; bizarre grossly inappropriate behaviour and/or disorganised behaviour with a marked deterioration in function.[410]

5.5.6.4. Childhood Experiences of Care and Abuse Questionnaire

The Childhood Experience of Care and Abuse Questionnaire or CECA-Q[401] is a questionnaire based on a semi structured interview: the Childhood Experience of Care and Abuse (CECA).[411] The CECA interview is designed to measure childhood experiences of neglect, antipathy, physical abuse and sexual abuse reported retrospectively.

The CECA-Q is a self-report tool based on the CECA interview. It has been found to have high reliability and validity.[401] It consists of six sections: parental loss; parental neglect; parental antipathy; support; physical punishment; and unwanted sexual experiences (Appendix J). A cumulative score for each section is obtained by adding a point for each item marked positive for adversity (some items are reversed). The CECA-Q has published cut-off scores to ensure that minor levels of adversity are not included.[412] These scores are then used to indicate the presence of childhood adversity. This is then used in the analyses to indicate: i) the presence or absence or childhood adversity and; ii) the number of different types of abuse (e.g. if neglect and physical abuse are both present, this would count as two types of abuse).

Due to the sensitive nature of the information needed for the completion of the CECA-Q, special measures were taken in the collection of this data. Participants were reminded of the confidential nature of the interview, were reminded that they were able to decline to answer any questions they felt uncomfortable with and were able to stop the interview at any point. If participants became distressed during the interview, they were offered tissues and the interviewer remained silent to give the participant time to compose themselves. Interviewers then clarified whether the participant wanted to continue before doing so. If participants were particularly distressed during the interview, they were advised to contact their GP or care coordinator.

5.5.6.5. Life Events and Difficulties Schedule

The Life Events and Difficulties Schedule (LEDS)[402, 403] is a semi-structured interview which is used to gather information on the presence or absence of a range of stressful life events and on-going difficulties (Appendix K).[413]

The LEDS is based on detailed definitions of what should and should not be included as an event or difficulty. This helps to ensure consistency between different studies but also guards against investigator bias that might arise were the inclusion of incidents determined retrospectively by the investigator. The LEDS events included are defined as incidents which would be followed by a negative or positive emotional response in most people, and are restricted to the participant and the participant's 'close ties' (partner, parent, sibling, child or close confidant).[414]

The LEDS list contains 40 types of event that fit into eight groups: changes in role for the participant; major changes in role for close ties; major changes in participants health; major changes in health for close ties; residence changes or marked change in

amount of contact with close ties; forecasts of change; fulfilments or disappointments of a valued goal; and other dramatic event involving the participant or close tie.[414] There are detailed manuals explaining the inclusion rules and glossaries of several hundreds of events and difficulties with their ratings.

Participants are first asked about the presence and timing of an event or difficulty.[413] In order to establish when the event had occurred, an anchor is provided to participants (e.g., bank holidays, birthdays etc.) to help them pinpoint the event more accurately.[414] The questioning is standardised only in that there are a list of topics to be discussed and a number of suggested probes. Once the presence or absence of an event or difficulty has been established, the interviewer explores the context of the event/difficulty.[413]

Once the information has been collected from the participant, a LEDS rating meeting is held.[414] During this, the participant interviewer reads an account of the event/difficulty and its surrounding circumstances (the 'context' of the event) to the rest of the research team. Care is taken to omit any mention of the participant's reaction to the event/difficulty and to omit any information on the subsequent incidence of illness.[414] A rating of contextual threat is then made independently by each member of the team without discussion. This threat rating is based on what most people would be likely to feel in response to the event given the particular circumstances (i.e. context) in which it occurred.[414] Ratings by members of the team are compared and any disagreements are discussed until a consensus rating is reached.

Short term threat for an event is defined as on the day of the event.[414] Long term threat for an event is a week after the occurrence. Long term difficulties are defined as difficulties of at least four weeks.[414] The rating of degree of threat for events is: marked;

moderate; some; and little or none. The rating of degree of threat for difficulties is on a scale of one to seven of unpleasantness with one indicating the highest degree of threat.[413] A severe event is one with marked or moderate long-term threat that is focussed on the participant only or jointly on the participant and one of the restricted list of close family/friends. A severe difficulty is one rated on the top three levels on the 7-point difficulty scale. Within this thesis, only severe events and difficulties were included.

Independence of an event or difficulty is also important. An independent event is when the event is independent of the case's mental state and unlikely to be the results of a behavioural change that might be linked to the onset of disorder. Within this thesis, only independent events and difficulties were used.

The LEDS was chosen for this study due to its advantages over other life events data collection methods. These are that the LEDS has greatly reduced 'false positives' (i.e., the number cases who claim to have life events but these events are not seen as significant from an objective point of view), it can overcome lack of awareness in cases (cases may underplay certain events which could be seen as significant from an objective point of view), it does not rule out using the person's view of the significance of the event, and checklist-dictionary approaches have been shown to have low validity and reliability.[414] Dohrenwend et al.[415] claim that the contextual approach adopted by the LEDS is more precise than the commonly used checklist methods. Brown and Harris[414] point out that there are no satisfactory alternatives.

5.5.6.6. Family Interview for Genetic Studies

Data on family history of mental illness was collected using the Family Interview for Genetic Studies (FIGS; see Appendix L).[416] The FIGS is a schedule for gathering diagnostic information about relatives of a proband within a study.[417] It can be conducted with the proband or a relative of the proband. The FIGS is made up of three parts: the family tree; general screening questions, and the symptom checklists. As a minimum, the family tree must include the proband's parents, grandparents, siblings, aunts, uncles, cousins, offspring and spouse.[418] The screening questions are then used to gather information on possible mental illness in first degree relatives. The symptom checklists are then used to elicit specific information about relatives that have an indication of mental illness from the screening questions. Within this study, a shortened version of the FIGS was used including the family tree, the general screening questions, and only the depression, mania and psychosis symptom checklists.

The information gathered using the FIGS was presented in consensus meetings (as described in section 5.5.7) to determine presence of mental illness and psychosis in parents and family members.

5.5.6.7. Control Measures

Control participants were asked to complete the same battery of assessments as the psychosis cases with the exception of the illness related questionnaires; Schedules for Clinical Assessment in Neuropsychiatry (SCAN)[399]; and the Personal and Psychiatric History Schedule (PPHS).[400]

5.5.7. Reliability

To ensure a high level of interrater reliability for the SCAN, all members of the research team who utilised the SCAN had to attend a one week formal World Health Organisation (WHO) training course. This ensured all raters were conducting and rating the SCAN in a standardised way. Interrater reliability of the SCAN was assessed using taped SCAN interviews with a Cohen's kappa coefficient ranging between 0.727 and 0.743.

Using information obtained via the SCAN, case notes and informant information, an ICD-10[14] diagnosis was determined by consensus using the following procedure. The researcher who completed the SCAN presented the information from the SCAN during a consensus meeting that was attended by at least 3 members of the research team, including at least one of the principal investigators. The presenter was very careful not to reveal information about the diagnosis given by the clinical team, or about the patient's ethnicity (as far as possible). Diagnosis was determined by consensus and any disagreement was resolved by discussion among the team. Interrater reliability between the London and Nottingham teams was estimated using 20 cases and was judged satisfactory by the research team, with Cohen's kappa coefficients ranging between 0.63 and 0.75 ($p<0.001$).

For all other schedules used within the study, formal standardised training was provided to each research team member before they began collecting data.

5.5.8. Ethical Issues

Ethical approval was granted for the baseline study by the Institute of Psychiatry and South London and Maudsley (SLaM) Research Ethics Committee for the London site,

by the City Hospital Research Ethics Committee for the Nottingham site and by the Bristol NHS Research Ethics Committee for the Bristol site.

As discussed in section 5.5.2.1, informed consent was sought from all participants. If a participant was judged not to have capacity to consent, they were not interviewed but still included in the study. This was made possible by the use of clinical notes which was authorised by the relevant ethics committees.

Confidentiality of data was strictly maintained by the use of participant identification numbers instead of names on paper copies of data and in databases. All databases were password protected and encrypted. Confidentiality was only broken in cases where there was a risk to the participant or others. In this case, a principle investigator was consulted and a clinician relevant to the participant (i.e. consultant psychiatrist, care coordinator, or GP) was contacted.

5.5.9. Data Management

All data were entered into Microsoft Access 2003[419] and a number of cleaning checks were run on the data. Any discrepancies were checked against the paper copies of the relevant measure and where necessary (and appropriate), corrected.

5.5.10. Statistical analyses

Mills[373] highlights the issues surrounding data analysis in terms of 'data torturing'. This means that if manipulated in enough different ways, the data can show anything the analyser wishes it to and can be used as evidence of whatever the investigator wants to prove. Thus, it is important to have a detailed analysis plan before attempting to analyse

data. This can aid the analyser to resist the urge to ‘mine the data’ for significant findings.

Statistical analysis of the data was conducted using Stata Version 10.[420]

5.5.10.1. Descriptive

The descriptive section took the following form: an account of the numbers of cases and controls recruited in to the study; a description of the demographic and clinical characteristics of the whole sample, and of the individual diagnostic groups of interest; a statistical comparison of demographic and clinical characteristics between cases and controls, and each of the individual diagnostic groups of interest. A comparison between cases and controls, and between the individual diagnostic groups of interest, on missing data was also conducted.

Description of demographic and clinical characteristics took the form of: means and standard deviations for variables which were interval/ratio, continuous and normally distributed;[421] medians and interquartile ranges for variables which were interval/ratio, continuous but not normally distributed;[421] and numbers and percentages for categorical variables.[421]

Statistical comparison tests between two groups (cases and controls) took the form of: independent sample t-tests for variables which were interval/ratio, continuous and normally distributed; Mann Whitney-U tests for variables which were interval/ratio, continuous and not normally distributed; and chi-squared tests for data which was categorical (including the use of the fisher’s exact test for variables which had expected numbers of less than 5 in a group).[422]

Statistical comparisons between more than two groups (between the diagnostic groups) took the form of: ANOVAs for variables which were interval/ratio, continuous and normally distributed; Kruskal-Wallis tests for variables which were interval/ratio, continuous and not normally distributed; and chi-squared tests for data which was proportional in nature (including the use of the fisher's exact test for variables which had expected numbers of less than 5 in a group). [422]

5.5.10.2. Analysis of risk factors

The analysis of risk factors has been broken down into two parts: unadjusted and adjusted analyses.

5.5.10.2.1. Unadjusted analyses

As it is not possible to calculate risk ratios in case control studies (as the controls form an unknown proportion of the total population at risk), odds ratios are the preferred measure of effect. As the outcome variable had more than 2 levels (categories),[423] multinomial logistic regressions were used. This allows for the comparison of each group to the control group to be conducted within a single regression model.

Within the multinomial regression analyses, data were weighted. If a random sample of the population is recruited, as was done for the controls, there are rarely enough ethnic minority individuals and for this study, there were not enough Black Caribbean participants. Therefore, Black Caribbean controls were oversampled. Analyses were therefore weighted to take account of this oversampling.

5.5.10.2.2. Adjusted analyses

Hennekens and Buring argue that "... age and sex are associated with virtually all diseases and are related to the presence or level of many exposures... This means that there must be an association between the confounder and disease even among non-exposed individuals."[424] Therefore, it is important to control for these within studies of risk factors. As well as age and gender, the analyses control for centre and ethnicity.

The possible ways to control for confounding are restriction, matching and analytical adjustments.[424] Restriction and matching both have limitations[424] and are only applicable at the design stage of the study. As the data had already been collected at the start of this thesis, I was limited to analytical adjustments. The analytical adjustment options are stratification and multivariate analyses. "A fundamental problem with stratified analysis, however, is its inability to control simultaneously for even a moderate number of potential confounders", thus multivariable analyses have been used to control for the key confounders.[424]

5.5.10.3. <u>General statistical issues</u>

Kirkwood and Sterne state that the questions that are trying to be answered in epidemiology are: 'what is the effect size?'; 'what does the effect in the study tell us about the size of the effect more generally in the population?; and 'do the data provide evidence that the observed difference may have arisen by chance?'. Researchers are aided in answering each of these questions through the use of measures of effect size (odds ratios, relative risk, incidence rate ratios), measures of precision (confidence intervals), and measures of chance (p-values).[425] Only with all three of these pieces of information can a researcher interpret the study findings. Therefore, the risk results chapter reported on all three of these components for each analysis: effect size;

confidence intervals; and p-values. Within the analyses and interpretation of the results, a p-value of less than 0.1 was taken to be indicative of weak evidence of an effect, a p-value of less than 0.05 was taken to be an indication of moderate evidence of an effect, and a p-value of less than 0.01 was taken to be an indication of strong evidence of an effect.

The recommendation that two-sided p values are used in epidemiological analyses because they cater for the uncertainty about the direction of effects[424] was adopted.

As stated in Chapter 3, diagnoses received at the time of onset are often inaccurate. Therefore analyses of risk factors based on initial diagnosis are likely to be misleading.[160] For this reason, all risk factor analyses were conducted on the baseline diagnoses, and then reanalysed using the lifetime diagnoses.

Within the analyses of risk factors, variables were simplified into binary factors where appropriate to simplify the analyses and increase power.

5.5.10.4. Power calculations

The data for this section of the thesis was collected prior to the thesis starting and thus numbers of cases and controls were not adjustable. However, a power calculation was conducted using NQuery Advisor[426] to determine what size of effects could be detected by the data. As there were many statistical tests, the power calculation was based on one of the comparisons: a comparison of PMD cases versus controls on the risk factor of relationship status (single versus not). A two group chi-square test with a 0.05 two-sided significance level was found to have 87% power to detect a difference between Group 1 (controls) with a proportion of 0.400 (40% single) and Group 2 (PMD cases) with a

proportion of 0.600 (60% single; odds ratio of 2.250) when the sample sizes are 381 and 69, respectively (a total sample size of 451).

5.6. Phase 2 – cohort study

The purpose of the cohort study was to enable an investigation of the course and outcome of PMD and SAD cases, and to test the hypotheses outlined at the end of Chapter 4.

5.6.1. Design

The cohort study aimed to follow-up all incidence cases identified in the case control study. Follow-up occurred at approximately 10 years after first presentation.

5.6.2. Participants

5.6.2.1. Cases

All cases identified in the incidence study were traced. Information from case notes and informants (psychiatrists and care coordinators) was gathered to complete the WHO Life Chart (see section 5.6.4.2). Once this had been completed, all traced cases were approached and invited to complete a battery of follow-up assessments including providing corroborative information for the life chart. Prior to participation, all participants were given a consent form (Appendix L). This was read to all cases and they had the opportunity to ask questions. All interviewed participants gave written informed consent.

5.6.3. Recruitment

Recruitment happened in three chronological stages:

1. SLaM services were approached to find out which cases were in contact with services. If a case was found to be in contact with services we approached that participant though their clinical team. If a case had been transferred to an out of area mental health service, we approached the participant through the relevant clinical team.
2. At baseline contact details were collated for each case. This information was used to write to the last known address. If no response was received after sending 2 letters, we visited the address. If this was unsuccessful, we contacted the last known GP in order to get a letter forwarded to the current address.
3. The details of all cases were run through ONS to gather information on who had died during follow-up.

5.6.4. Measures

As reported in section 5.6.2.1, data was collected using a combination of self-reported information, clinical notes and information from informants. Clinical notes were used to collect information on core items such as course of illness, months of remission, suicide attempts, social outcomes and service use among many others. Cases who consented to be interviewed were then asked to complete a battery of assessments. Table 5-7 lists the assessments that were used in this thesis. Within this thesis, the only measures which were used were the Schedules for Clinical Assessment in Neuropsychiatry, Version 2 (SCAN, V2)[399] and the WHO Life Chart schedule.[427, 428]

5.6.4.1. Schedules for Clinical Assessment in Neuropsychiatry

Details on the SCAN have already been given in section 5.5.6.2. The SCAN[399] was used to determine the present mental state at follow-up, i.e. the one month prior to the interview.

As at baseline, information obtained from the SCAN, case notes, informant information and the Life Chart were presented at consensus meetings (see section 5.5.7) to determine a lifetime diagnosis. These consensus meetings involved at least 3 members of the research team including at least one who was a consultant psychiatrist. The lifetime diagnosis was made according to the ICD-10[14] and as far as possible, blind to baseline diagnosis and ethnicity.

Table 5-7: Follow-up assessments

Type of data	Schedule	Source of data
Clinical	Schedules for Clinical Assessment in Neuropsychiatry Version 2 (SCAN, V2)[399]	Patient
Clinical Social Service use	WHO Life Chart[429, 430]	Patient Case notes Other informants

Amended from Morgan et al., 2006[380]

5.6.4.2. WHO Life Chart Schedule

The WHO Life Chart Schedule[429, 430] was designed to assess the long-term course of schizophrenia.[430] It includes four main areas; symptoms; treatment; residence; and work. The Life Chart in this study was adapted to include more information on service use (relevant parts of the Life Chart are included in Appendix N).

Information was derived for the life chart from a combination of sources: case notes and, when possible, interviews with cases and informant information (carers, relatives, friends, GPs, treating consultants).

From the Life Chart, the following information was gathered for this thesis: course of illness (episodic (defined as no episode lasting over 6 months), continuous (defined as no remission lasting over 6 months) or 'neither episodic nor continuous' (episodes lasted over 6 months and remission lasted over 6 months); longest period of remission; average number of episodes; months of longest episode; percentage of time psychotic during follow-up; deaths; completed suicide; attempted suicide; self-harm; time in prison; relationship status; employment status; close confidants; binary hospitalisations; total number of hospitalisations; total number of days hospitalised; proportion of the follow-up spent as an inpatient; percentage of admissions which were compulsory; having ever been admitted compulsorily; and percentage of hospitalisations involving the police. As well as being used to inform decisions about lifetime diagnoses (see section 5.6.5), the Life Chart was also presented at consensus meetings along with case note information so decisions about all aspects of the Life Charts could be decided upon in a consensus fashion.

5.6.5. Reliability

As with the case control study, to ensure a high level of interrater reliability in the SCAN, all members of the cohort research team who used the SCAN attended a one week formal WHO training course to ensure all raters were conducting and rating the SCAN in a standardised way. On all other schedules used within the study, formal standardised training was provided to each research team member before they began

collecting data. As mentioned above, completion of the Life Chart and decisions about diagnosis were made by the team in consensus meetings to improve reliability.

5.6.6. Ethical Issues

Ethical approval was granted by the Institute of Psychiatry and SLaM Research Ethics Committee (reference 321/02) for the London site and by the North Nottinghamshire Local Research Ethics Committee (reference 04/Q2402/35) for the Nottingham site. Informed consent was sought from all participants. If a participant was judged not to have capacity to consent, they were not interviewed.

As with the case control study, confidentiality of data was strictly maintained by the use of participant identification numbers instead of names on paper copies of data and in databases. All databases were password protected and encrypted. Confidentiality was only broken in cases where there was a risk to the participant or others. In any such case, a principle investigator was consulted and a clinician relevant to the participant (i.e. consultant psychiatrist, care coordinator, or GP) was contacted, and a relevant report was made to the local ethics committee.

5.6.7. Data Management

All life chart data was double entered. A number of cleaning checks were also run on the data. Any discrepancies were checked against the paper copies of the relevant measure.

5.6.8. Statistical analyses

All data was analysed in STATA 10.[431] Outcome variables were described using means and standard deviations where variables were interval/ratio, continuous and normally distributed,[421] medians and interquartile ranges where variables were interval/ratio, continuous but not normally distributed,[421] and numbers and percentages for categorical variables.[421] Categorical variables with more than two levels were transformed into binary variables (where appropriate) to simplify analyses and their interpretation (e.g. married and cohabiting were combined into an 'in a relationship' group and single, divorced, separated and widowed were all combined into a 'single' group).

As the focus of the outcomes analyses was to investigate the course and outcomes of PMD and SAD cases compared with bipolar disorder and schizophrenia cases, the following comparisons were made: PMD versus schizophrenia; PMD versus bipolar disorder; PMD versus SAD; SAD versus schizophrenia; SAD versus bipolar disorder. To conduct comparisons in binary categorical outcome variables, logistic regression was employed, using the 'or' option to create odds ratios (ORs).[421] ORs are almost always reported in medical literature when analysing binary variables.[425] This is for the three key reasons: when the outcome is rare, the odds ratio is the same as the risk ratio; when the outcome is common, risk ratios are constrained but the odds ratio are not; and for odds ratios, the conclusions are identical whether we consider our outcome as the occurrence of an event, or the absence of the event.[425] For these reasons, odds ratios are being used to measure the effect sizes in the cohort study.

For continuous interval and ratio data which were normally distributed, linear regression was used.[421] However, post regression, residuals were examined using the graph box, 'kdensity', 'pnorm' and 'qnorm' commands in STATA to examine the normality of the residuals.[432] These outputs were judged by visually analysing the outputs. For variables

where the residuals were normal, the linear regression was used. For interval/ratio, continuous, normally distributed outcomes for which the residuals were not normal, or for outcome variables which were non-normally distributed, the 'Ladder' function was used to indicate which transformation would produce the most normal distribution.[432] Once the variable was transformed, a linear regression was used plus the checking for normality process mentioned above was again adopted. If transformation did not correct normality problems, then a bootstrap regression (using 1000 replications) was implemented.[423] Bootstrapping is a non-parametric statistical method which accounts for the skewedness of the data.[433] It is, therefore, suitable for use when the normality assumption is violated. Bootstrapping is primarily used when distributions are skewed and when sample sizes are modest.[433]

For outcome variables which were count data, poisson regression was used.[423] A calculation of incidence-rate ratios was conducted using the 'irr' option in STATA. Since the poisson command assumes all subjects had the same follow-up time, the 'exposure' option was used to indicate the length of time an individual was followed for to adjust the poisson regression estimates.[434] The 'vce(robust)' option was also used to obtain robust standard errors for the parameter estimates in order to control for mild violation of underlying assumptions.[435] However, where count data was not normally distributed, the dispersion of the data was tested by examining the mean and variance.[436] Where the variance was similar to or the same as the mean, this indicated over dispersion was not present and poisson regression was used. Where the variance was greater than the mean, this indicated over dispersion and therefore, negative binomial regression was used.[437] As with the poisson regression, incident rate ratios were calculated and the 'exposure' option was used to adjust regression estimates according to follow-up time.

As with the analysis of the risk factors in the case control study, results were presented in the following way: effect size; confidence intervals; p-values. In addition, as with the case control analyses, a more liberal p value of <0.1 has been employed, two-tailed tests have been utilised and analyses were run first based on the baseline diagnoses and then on the lifetime diagnoses.

5.6.8.1. Power calculations

The data for this section of the thesis was dictated by the number of cases collected in the case control section of the study and thus the numbers of cases, and numbers of specific diagnoses were not adjustable. However, a power calculation was conducted using NQuery Advisor[426] to determine what size of effects could be detected by the data. As there were many statistical tests, the power calculation was based on one of the comparisons: a comparison of PMD cases and schizophrenia cases in the outcome of episodic versus other illness course type. A two group chi-square test with a 0.050 two-sided significance level would have 80% power to detect a difference between Group 1 (schizophrenia cases) with a proportion of 0.200 (20% of cases episodic) and Group 2 (PMD cases) with a proportion of 0.400 (40% of cases episodic; odds ratio of 2.667) when the sample sizes are 167 and 51, respectively (a total sample size of 218).

CHAPTER 6. Results of social adversity risk factors for PMD and SAD

"... differential exposure to stressful life events is substantially less important than differential vulnerability to stress in determining the relationships between mental health and social class, gender, and marital status."[70]

Turner, Wheaton and Lloyd (1995)

6.1. Aims of the chapter

The aim of this chapter was to describe the baseline characteristics of the sample under examination in this thesis and to examine the social adversity risk factors described in chapter 3. As this thesis aimed to improve on previous research by examining risk factors by both baseline and lifetime diagnosis, diagnostic change will be briefly described in this chapter, but fully explored in chapter 7. A comparison of differences in findings by baseline and lifetime diagnosis will be discussed in chapter 8.

6.2. Baseline sample characteristics

6.2.1. Numbers

A total of 511 first episode psychosis cases were identified at baseline. During the follow-up phase of the study, it came to light that six cases did not meet the inclusion criteria at baseline as they were either not first episode at baseline or had an organic psychosis at baseline. These six cases were therefore excluded from the baseline analyses which led to a total number of 505 cases. These 505 cases consisted of 304 from the London site and 201 from the Nottingham site. Over, the 2-year period from 1st September 1997 to the 31st August 1999 in which all eligible cases were included in the study, a total of 444 were identified. A further 61 participants were identified during the leakage phase of the study. A total of 391 controls were recruited, 183 from London and 208 from Nottingham.

6.2.2. Demographic and clinical variables for the total sample

A description of the baseline demographic characteristics for cases compared with controls is shown in Table 6-1. From this table it can be seen that there was evidence

that cases were different from the controls on all demographic variables except place of birth (Table 6-1). This is to be expected as sociodemographic variables are often associated with disease.[424] This is not further explored here as these variables are included in the risk factors analysis and so are further explored in section 6.3.

Table 6-1: Overall demographic variables for cases versus controls at baseline

	Cases (n=505)	**Controls (n=391)**		
	Median (IQR)	***Median (IQR)***	***Mann-Whitney U***	***P-value***
Age	29.00 (22-36)	35.00 (28-47)	8.295	<0.001
	N (%)	***N (%)***	***Chi2, df***	***P-value***
Study centre:				
London	304 (60.2)	183 (46.8)	15.94, 1	<0.001
Nottingham	201 (39.8)	208 (53.2)		
Gender:				
Male	293 (58.0)	161 (41.2)	25.01, 1	<0.001
Female	212 (42.0)	230 (58.8)		
Ethnicity:				
White British	228 (45.2)	241 (61.6)	48.41, 5	<0.001
African-Caribbean	119 (23.6)	74 (18.9)		
Black African	65 (12.9)	21 (5.4)		
White Other	36 (7.1)	42 (10.7)		
Asian	26 (5.2)	8 (2.0)		
Other (all)	31 (6.1)	5 (1.3)		
Place of birth:				
UK	368 (73.9)	307 (78.5)	2.56, 1	0.110
Non-UK	130 (26.1)	84 (21.5)		
Living circumstances:				
Others	274 (54.8)	270 (69.1)	18.75, 1	<0.001
Alone	226 (45.2)	121 (31.0)		
Relationship Status:				
Steady relationship	133 (27.5)	238 (60.9)	98.73, 1	<0.001
Single	351 (72.5)	153 (39.1)		
Employment Status:				
Other	178 (36.6)	232 (59.3)	45.23, 1	<0.001
Unemployed	309 (63.5)	159 (60.7)		
Level of Education:				
School	295 (60.2)	179 (46.1)	24.09, 2	<0.001
Further	131 (26.7)	114 (29.4)		
Higher	64 (13.1)	95 (24.5)		

Some variables have missing cases (see Table 6-5). IQR = Interquartile range.

Table 6-2 presents the clinical variables for the cases. From this table, it can be seen that the most common baseline ICD-10 diagnosis was schizophrenia. There were 72 PMD cases and 21 SAD cases.

Table 6-2: Overall clinical variables for all cases at baseline

	Cases (n505)
	Median (IQR)
DUP in days	59 (15-231)
Age of onset	27.50 (21-35)
	N (%)
Baseline ICD-10 diagnosis:	
Schizophrenia	218 (43.2)
PMD	72 (14.3)
BP/Mania	70 (13.9)
SAD	21 (4.2)
SABP/SAM	10 (2.0)
Other / Unspecified nonorganic disorder	36 (7.1)
Acute and transient psychosis	29 (5.7)
Drug / alcohol induced psychosis	26 (5.2)
Delusional disorder	22 (4.4)
Schizotypal disorder	1 (0.2)
Mode of Onset:	
Sudden	63 (14.3)
Precipitous	29 (6.6)
Acute, no previous symptoms	59 (13.4)
Acute, with previous symptoms	61 (13.8)
Insidious	216 (48.9)
No clear line of demarcation	14 (3.2)
Contact initiated by:	
Self	136 (29.4)
Family	156 (33.8)
Friends	23 (5.0)
Police	52 (11.3)
Prison/Court	24 (5.2)
Other	71 (15.4)
Source of Referral:	
GP	179 (36.2)
A&E	103 (20.9)
EC: self	20 (4.1)
EC: family/friends	25 (5.1)
Police	81 (16.4)
Prison/Courts	22 (4.5)
Social services	17 (3.4)
Via Psychiatric Home Visit	25 (5.1)
Other	22 (4.5)
Initial Mode of Contact:	
Community Patient	157 (31.7)
Voluntary Inpatient	159 (32.1)
Compulsory Inpatient	180 (36.3)

Some variables have missing cases (see Table 6-6). IQR = Interquartile range.

The groups of interest, PMD and SAD, were compared with the other major diagnostic groups, schizophrenia and bipolar disorder. Cases with a diagnosis of a manic episode with psychotic symptoms (F30) or bipolar affective disorder with psychotic symptoms (F31) were both included as bipolar disorder. The remaining diagnoses were not used in the risk factor analysis as they were not the focus of this thesis and the low numbers

were considered a power problem. Therefore, they are not included in the rest of this chapter. Removal of these cases resulted in a total number of cases in the four key diagnostic groups of 381.

A description of the baseline demographic characteristics comparing the four key diagnostic groups is presented in Table 6-3. From this table, it can be seen that there was evidence that the diagnostic groups were different from each other in terms of age, centre, gender, ethnicity, relationship status and education level. A post hoc analysis has not been conducted to examine between which diagnostic groups the differences in these variables exist as the focus of the risk factors analysis is on whether the risk factors for each diagnostic group compared with controls, and this is explored in section 6.3.

Table 6-4 shows the clinical variables by different diagnoses. It shows that there was evidence of a difference between the diagnostic groups for all the clinical variables. A post hoc analysis has not been conducted to examine where the differences in these variables between the diagnostic groups exist in clinical variables as this was beyond the scope of what was feasible in this thesis.

The demographic and clinical variables above were intended to characterise the sample and as such are as detailed as possible. A number of these variables were modified in order to simplify the analyses and increase power. These modified variables are used henceforth and are described in chapter 5.

Table 6-3: Overall demographic variables for cases divided by baseline diagnoses

	PMD (n72)	**SAD (n21)**	**Schizophrenia (n218)**	**Bipolar (n70)**		
	Median (IQR)	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***	***Kruskal Wallis, df***	***P value***
Age	32.50 (25-41)	28.00 (24-38)	29.00 (22-35)	27.00 (23-33)	7.938, 3	0.047
	N (%)	***N (%)***	***N (%)***	***N (%)***	***Chi2, df***	***P value***
Study centre:						
London	35 (48.6)	13 (61.9)	151 (69.3)	44 (62.9)	10.069, 3	0.018
Nottingham	37 (51.4)	8 (38.1)	67 (30.7)	26 (37.1)		
Gender:						
Male	36 (50.0)	13 (61.9)	140 (64.2)	33 (47.1)	8.878, 3	0.031
Female	36 (50.0)	8 (38.1)	78 (35.8)	37 (52.9)		
Ethnicity:						
White British	37 (51.4)	14 (66.7)	81 (37.2)	27 (38.6)	30.696, 15	0.010 (Fisher's exact)
African-Caribbean	8 (11.1)	2 (9.5)	61 (28.0)	14 (20.0)		
Black African	7 (9.7)	4 (19.1)	33 (15.1)	11 (15.7)		
White Other	4 (5.6)	0	22 (10.9)	4 (5.7)		
Asian	7 (9.7)	1 (4.8)	10 (4.6)	6 (8.6)		
Other (all)	9 (12.5)	0	11 (5.1)	8 (11.4)		
Place of birth:						
UK	50 (69.4)	16 (76.2)	148 (69.8)	53 (76.8)	1.622, 3	0.654
Non-UK	22 (30.6)	5 (23.8)	64 (30.2)	16 (23.2)		
Living circumstances:						
Others	45 (64.3)	9 (42.9)	114 (52.8)	38 (54.3)	4.110, 3	0.250
Alone	25 (35.7)	12 (57.1)	102 (47.2)	32 (45.7)		
Relationship Status:						
Steady relationship	28 (40.6)	5 (23.8)	40 (19.4)	25 (35.7)	15.342, 3	0.002
Single	41 (59.4)	16 (76.2)	166 (80.6)	45 (64.3)		
Level of Education:						
School	46 (66.7)	11 (55.0)	130 (61.3)	28 (40.6)	14.617, 6	0.018 (Fisher's exact)
Further	12 (17.4)	6 (30.0)	58 (27.4)	25 (36.2)		
Higher	11 (15.9)	3 (15.0)	24 (11.3)	16 (23.2)		
Employment Status:						
Other	34 (48.6)	7 (35.0)	68 (32.5)	30 (42.9)	6.752, 3	0.080
Unemployed	36 (51.4)	13 (65.0)	141 (67.5)	40 (57.1)		

Some variables have missing cases (see Table 6-5). IQR = Interquartile range.

Table 6-4: Overall clinical variables for cases divided by baseline diagnoses

	PMD (n72)	**SAD (n21)**	**Schizophrenia (n218)**	**Bipolar (n70)**		
	Median (IQR)	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***	***Kruskal Wallis, df***	***P value***
DUP in days	41.50 (15.00-123.00)	51.00 (17.00-92.00)	123.50 (31.00-443.00)	21.00 (7.00-66.00)	48.829, 3	<0.001
Age of onset	34.00 (23.00-41.00)	27.50 (23.50-36.00)	27.00 (20.00-34.00)	28.00 (23.00-33.00)	10.436, 3	0.015
	N (%)	***N (%)***	***N (%)***	***N (%)***	***Chi2, df***	***P value***
Mode of Onset:						
Sudden	4 (6.3)	0 (0.0)	19 (10.2)	15 (23.4)	51.821, 15	<0.001 (fisher's exact)
Precipitous	6 (9.4)	1 (5.3)	6 (3.2)	11 (17.2)		
Acute, no previous symptoms	6 (9.4)	3 (15.8)	24 (12.8)	11 (17.2)		
Acute, with previous symptoms	12 (18.8)	2 (10.5)	19 (10.2)	13 (20.3)		
Insidious	35 (54.7)	13 (68.4)	109 (58.3)	14 (21.9)		
No clear line of demarcation	1 (1.6)	0	10 (5.4)	0		
Contact initiated by:						
Self	23 (35.4)	11 (61.1)	54 (27.4)	11 (16.7)	41.224, 15	<0.001 (fisher's exact)
Family	24 (36.9)	3 (16.7)	60 (30.5)	30 (45.5)		
Friends	3 (4.6)	1 (5.6)	9 (4.6)	4 (6.1)		
Police	3 (4.6)	1 (5.6)	17 (8.6)	15 (22.7)		
Prison/Court	2 (3.1)	0	16 (8.1)	3 (4.6)		
Other	10 (15.4)	2 (11.1)	41 (20.8)	3 (4.6)		
Source of Referral:						
GP	38 (55.1)	8 (40.0)	77 (36.2)	14 (20.6)	48.167, 24	<0.001 (fisher's exact)
A&E	8 (11.6)	7 (35.0)	44 (20.7)	16 (23.5)		
EC: self	2 (2.9)	2 (10.0)	9 (4.2)	3 (4.4)		
EC: family/friends	4 (5.8)	0	10 (4.7)	4 (5.9)		
Police	6 (8.7)	1 (5.0)	29 (13.6)	22 (32.4)		
Prison/Courts	0	0	16 (7.5)	3 (4.4)		
Social services	4 (5.8)	1 (5.0)	11 (5.2)	0		
Via Psychiatric Home Visit	5 (7.3)	0	10 (4.7)	4 (5.9)		
Other	2 (2.9)	1 (5.0)	7 (3.3)	2 (2.9)		
Initial Mode of Contact:						
Community Patient	26 (37.1)	8 (38.1)	72 (33.8)	9 (13.2)	45.207, 6	<0.001
Voluntary Inpatient	34 (48.6)	11 (52.4)	59 (27.7)	17 (25.0)		
Compulsory Inpatient	10 (14.3)	2 (9.5)	82 (38.5)	42 (61.8)		

Some variables have missing cases (see Table 6-6). IQR = Interquartile range.

6.2.3. Missing data

Table 6-5 and Table 6-6 show the differences in missing data for each risk factor variable used in the adjusted and unadjusted analyses comparing cases and controls and diagnostic groups respectively. Table 6-5 shows evidence that there was a difference between the cases and controls in terms of missing data in most of the risk factor variables. This difference in missing data is to be expected due to the fact that controls volunteered themselves to be in the study and a replacement control was found when a control refused participation. Cases on the other hand were selected due to their being a case and an alternative could not be obtained. The potential bias resulting from missing data is discussed in chapter 8.

Table 6-6 shows that there are no differences in missing data between the diagnostic groups in most of the variables examined. However, there was evidence of differences between different diagnostic groups in lifetime relationship and employment statuses, family contacts, family mental health history and childhood adversity data. This has implications for the possibility of bias which are considered in chapter 8.

Table 6-5: Missing data in the risk factor variables by case and controls (baseline data)

	Cases (n=381)	**Controls (n=391)**		
	N (%)	***N (%)***	***Chi2, df***	***P value***
Age				
Present	381 (100)	391 (100)	-	-
Missing	0 (0)	0 (0)		
Study centre:				
Present	381 (100)	391 (100)	-	-
Missing	0 (0)	0 (0)		
Gender:				
Present	381 (100)	391 (100)	-	-
Missing	0 (0)	0 (0)		
Ethnicity:				
Present	381 (100)	391 (100)	-	-
Missing	0 (0)	0 (0)		
Place of birth:				
Present	374 (98.2)	391 (100)	7.250, 1	0.007 (fishers

	Cases (n=381)	**Controls (n=391)**		
	N (%)	***N (%)***	***Chi2, df***	***P value***
Missing	7 (1.8)	0 (0)		exact)
Living circumstances:				
Present	377 (99.0)	391 (100)	4.126, 1	0.059 (fishers
Missing	4 (1.1)	0 (0)		exact)
Relationship Status:				
Present	366 (96.1)	391 (100)	15.699, 1	<0.001
Missing	15 (3.9)	0 (0)		
Ever relationship				
Present	284 (74.5)	386 (98.7)	98.396, 1	<0.001
Missing	97 (25.5)	5 (1.3)		
Level of Education:				
Present	370 (97.1)	388 (99.2)	4.870, 1	0.027
Missing	11 (2.9)	3 (0.8)		
Employment Status:				
Present	369 (96.9)	391 (100)	12.510, 1	<0.001
Missing	12 (3.2)	0 (0)		
Ever worked				
Present	290 (76.1)	390 (99.7)	102.637, 1	<0.001
Missing	91 (23.9)	1 (0.3)		
Contact with friends:				
Present	250 (65.6)	378 (96.7)	122.675, 1	<0.001
Missing	131 (34.4)	13 (3.3)		
Contact with family:				
Present	256 (67.2)	368 (94.1)	90.286, 1	<0.001
Missing	125 (32.8)	23 (5.9)		
Close confidants:				
Present	291 (76.4)	388 (99.2)	95.131, 1	<0.001
Missing	90 (23.6)	3 (0.8)		
Family history of any mental illness:	276 (72.4)	391 (100)	124.719, 1	<0.001
Present	105 (27.6)	0 (0)		
Missing				
Family history of psychosis:				
Present	276 (72.4)	391 (100)	124.719, 1	<0.001
Missing	105 (27.6)	0 (0)		
Parental history of any mental illness:	276 (72.4)	391 (100)	124.719, 1	<0.001
Present	105 (27.6)	0 (0)		
Missing				
Parental history of psychosis:				
Present	276 (72.4)	391 (100)	124.719, 1	<0.001
Missing	105 (27.6)	0 (0)		
Life Events:				
Present	73 (19.2)	147 (37.6)	32.187, 1	<0.001
Missing	308 (80.8)	244 (62.4)		
Life Difficulties:				
Present	82 (21.5)	149 (38.1)	25.313, 1	<0.001
Missing	299 (78.5)	242 (61.9)		
Childhood Adversity:				
Present	144 (37.8)	242 (61.9)	44.821, 1	<0.001
Missing	237 (62.2)	149 (38.1)		
Number of Childhood Adversity Factors:	144 (37.8)	242 (61.9)	44.821, 1	<0.001
Present	237 (62.2)	149 (38.1)		
Missing				

Table 6-6: Missing data in the risk factor variables by diagnostic group (baseline data)

	PMD (n72)	**SAD (n21)**	**Schizophrenia (n218)**	**Bipolar (n70)**		
	N (%)	**N (%)**	**N (%)**	**N (%)**	***Chi2, df***	***P value***
Age						
Present	72 (100)	21 (100)	218 (100)	70 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Study centre:						
Present	72 (100)	21 (100)	218 (100)	70 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Gender:						
Present	72 (100)	21 (100)	218 (100)	70 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Ethnicity:						
Present	72 (100)	21 (100)	218 (100)	70 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Place of birth:						
Present	72 (100)	21 (100)	212 (97.3)	69 (98.6)	2.818, 3	0.623 (fisher's exact)
Missing	0 (0)	0 (0)	6 (2.8)	1 (1.4)		
Living circumstances:						
Present	70 (97.2)	21 (100)	216 (99.1)	70 (100)	3.072, 3	0.476 (fisher's exact)
Missing	2 (2.8)	0 (0)	2 (0.9)	0 (0)		
Relationship Status:						
Present	69 (95.8)	21 (100)	206 (94.5)	70 (100)	5.156, 3	0.184 (fisher's exact)
Missing	3 (4.2)	0 (0)	12 (5.5)	0 (0)		
Ever relationship						
Present	42 (82.4)	13 (68.4)	155 (68.9)	60 (82.2)	7.565, 3	0.052
Missing	9 (17.6)	6 (31.6)	70 (31.1)	13 (17.8)		
Level of Education:						
Present	69 (95.8)	20 (95.2)	212 (97.3)	69 (98.6)	1.229, 3	0.598 (fisher's exact)
Missing	3 (4.2)	1 (4.8)	6 (2.8)	1 (1.4)		
Employment Status:						
Present	70 (97.2)	20 (95.2)	209 (95.9)	70 (100)	3.173, 3	0.319 (fisher's exact)
Missing	2 (2.8)	1 (4.8)	9 (4.1)	0 (0)		
Ever worked						
Present	42 (82.4)	14 (73.7)	158 (70.2)	59 (80.8)	5.303, 3	0.157 (fisher's exact)
Missing	9 (17.6)	5 (26.3)	67 (29.8)	14 (19.2)		
Contact with friends:						
Present	52 (72.2)	13 (61.9)	132 (60.6)	53 (75.7)	7.164, 3	0.067
Missing	20 (27.8)	8 (38.1)	86 (39.5)	17 (24.3)		
Contact with family:						
Present	54 (75.0)	15 (71.4)	132 (60.6)	55 (78.6)	10.636, 3	0.014
Missing	18 (25.0)	6 (28.6)	86 (39.5)	15 (21.4)		
Close confidants:						
Present	59 (81.9)	14 (66.7)	159 (72.9)	59 (84.3)	6.192, 3	0.103
Missing	13 (18.1)	7 (33.3)	59 (27.1)	11 (17.7)		
Family history of any mental illness:	58 (80.6)	17 (81.0)	143 (65.6)	58 (82.9)	12.057, 3	0.007
Present	14 (19.4)	4 (19.1)	75 (34.4)	12 (17.1)		
Missing						
Family history of psychosis:	58 (80.6)	17 (81.0)	143 (65.6)	58 (82.9)	12.057, 3	0.007
Present	14 (19.4)	4 (19.1)	75 (34.4)	17 (17.1)		
Missing						

	PMD (n72)	SAD (n21)	Schizophrenia (n218)	Bipolar (n70)		
	N (%)	N (%)	N (%)	N (%)	*Chi2, df*	*P value*
Parental history of any mental illness: Present Missing	58 (80.6) 14 (19.4)	17 (81.0) 4 (19.1)	143 (65.6) 75 (34.4)	58 (82.9) 17 (17.1)	12.057, 3	0.007
Parental history of psychosis: Present Missing	58 (80.6) 14 (19.4)	17 (81.0) 4 (19.1)	143 (65.6) 75 (34.4)	58 (82.9) 17 (17.1)	12.057, 3	0.007
Life Events: Present Missing	21 (29.2) 51 (70.8)	3 (14.3) 18 (85.7)	34 (15.6) 184 (84.4)	15 (21.4) 55 (78.6)	6.997, 3	0.081 (fisher's exact)
Life Difficulties: Present Missing	22 (30.6) 50 (69.4)	4 (19.1) 17 (81.0)	40 (18.4) 178 (81.7)	16 (22.9) 54 (77.1)	4.928, 3	0.181 (fisher's exact)
Childhood Adversity: Present Missing	33 (45.8) 39 (54.2)	7 (33.3) 14 (66.7)	70 (32.1) 148 (67.9)	34 (48.6) 36 (41.4)	8.611, 3	0.035
Number of Childhood Adversity Factors: Present Missing	33 (45.8) 39 (54.2)	7 (33.3) 14 (66.7)	70 (32.1) 148 (67.9)	34 (48.6) 36 (41.4)	8.611, 3	0.035

6.3. Social adversity risk factors by baseline diagnosis

6.3.1. Unadjusted analyses

To test the hypothesis that psychosocial risk factors are associated with PMD and SAD, comparisons were made for each baseline diagnostic group (PMD and SAD plus the comparison groups of schizophrenia and bipolar disorder) compared with controls. This is shown in Table 6-7 and Table 6-8.

Table 6-7: Summary of potential risk factors for controls and each baseline diagnostic group

	Controls (n391)	PMD (n72)	SAD (n21)	Schizophrenia (n218)	Bipolar (n70)
	Median (IQR)	*Median (IQR)*	*Median (IQR)*	*Median (IQR)*	*Median (IQR)*
Age	35 (28-47)	32.5 (25-41)	28 (24-38)	29 (22-35)	27 (23-33)
	N (%)	*N (%)*	*N (%)*	*N (%)*	*N (%)*
Study centre: Nottingham London	 208 (53.20) 183 (46.80)	 37 (51.39) 35 (48.61)	 8 (38.10) 13 (61.90)	 67 (30.73) 151 (69.27)	 26 (37.14) 44 (62.86)
Gender:					

	Controls (n391)	PMD (n72)	SAD (n21)	Schizophrenia (n218)	Bipolar (n70)
Female	230 (58.82)	36 (50.00)	8 (38.10)	78 (35.78)	37 (52.86)
Male	161 (41.18)	36 (50.00)	13 (61.90)	140 (64.22)	33 (47.14)
Ethnicity:					
White British	241 (61.64)	37 (51.39)	14 (66.67)	81 (37.16)	27 (38.57)
African-Caribbean	74 (18.93)	8 (11.11)	2 (9.52)	61 (27.98)	14 (20.00)
Black African	21 (5.37)	7 (9.72)	4 (19.05)	33 (15.14)	11 (15.71)
White Other	42 (10.74)	4 (5.56)	0 (0.00)	22 (10.09)	4 (5.71)
Asian (all)	8 (2.05)	7 (9.72)	1 (4.76)	10 (4.59)	6 (8.57)
Other	5 (1.28)	9 (12.50)	0 (0.00)	11 (5.05)	8 (11.43)
Place of birth:					
UK	307 (78.52)	50 (69.44)	16 (76.19)	148 (69.81)	53 (76.81)
Non-UK	84 (21.48)	22 (30.56)	5 (23.81)	64 (30.19)	16 (23.19)
Relationship Status:					
Stable relationship	238 (60.87)	28 (40.58)	5 (23.81)	40 (19.42)	25 (35.71)
Single	153 (39.13)	41 (59.42)	16 (76.19)	166 (80.58)	45 (64.29)
Ever had a long term relationship:					
Yes	296 (76.68)	36 (62.07)	10 (58.82)	55 (36.91)	25 (41.67)
No	90 (23.32)	22 (37.93)	7 (41.18)	94 (63.09)	35 (58.33)
Living with:					
With people	270 (69.05)	45 (64.29)	9 (42.86)	114 (52.78)	38 (54.29)
Alone	121 (30.95)	25 (35.71)	12 (57.14)	102 (47.22)	32 (45.71)
Level of Education:					
Higher	95 (24.48)	11 (15.94)	3 (15.00)	24 (11.32)	16 (23.19)
Further	114 (29.38)	12 (17.39)	6 (30.00)	58 (27.36)	25 (36.23)
School	179 (46.13)	46 (66.67)	11 (55.00)	130 (61.32)	28 (40.58)
Employment Status:					
Employed and other	232 (59.34)	34 (48.57)	7 (35.00)	68 (32.54)	30 (42.86)
Unemployed	159 (40.66)	36 (51.43)	13 (65.00)	141 (67.46)	40 (57.14)
Ever worked					
Yes	383 (98.21)	57 (96.61)	16 (94.12)	141 (92.16)	57 (93.44)
No	7 (1.79)	2 (3.39)	1 (5.88)	12 (7.84)	4 (6.56)
Contact with friends:					
Daily – monthly	360 (95.24)	42 (80.77)	11 (84.62)	85 (64.39)	46 (86.79)
Never / less than monthly	18 (4.76)	10 (19.23)	2 (15.38)	47 (35.61)	7 (13.21)
Contact with family:					
Daily – monthly	359 (97.55)	50 (92.59)	12 (80.00)	124 (93.94)	53 (96.36)
Never / less than monthly	9 (2.45)	4 (7.41)	3 (20.00)	8 (6.06)	2 (3.64)
Close confidants:					
Yes	361 (93.04)	44 (74.58)	10(71.43)	84 (52.83)	44 (74.58)
No	27 (6.96)	15 (25.42)	4 (28.57)	75 (47.17)	15 (25.42)
Family history of any mental illness:					
No	360 (92.07)	41 (70.69)	10 (58.82)	88 (61.54)	33 (56.90)
Yes	31 (7.93)	17 (29.31)	7 (41.18)	55 (38.46)	25 (43.10)
Family history of psychosis:					
No	375 (95.91)	48 (82.76)	12 (70.59)	97 (67.83)	45 (77.59)
Yes	16 (4.06)	10 (17.24)	5 (29.41)	46 (32.17)	13 (22.41)
Parental history of any mental illness:					
No	380 (97.19)	49 (84.48)	14 (82.35)	112 (78.32)	45 (77.59)
Yes	11 (2.81)	9 (15.52)	3 (17.65)	31 (21.68)	13 (22.41)
Parental history of psychosis:					
No	384 (98.21)	52 (89.66)	15 (88.24)	117 (81.82)	51 (87.93)
Yes	7 (1.79)	6 (10.34)	2 (11.76)	26 (18.18)	7 (12.07)
Life Events					
No	109 (74.15)	8 (38.10)	1 (33.33)	23 (67.65)	8 (53.33)

	Controls (n391)	**PMD (n72)**	**SAD (n21)**	**Schizophrenia (n218)**	**Bipolar (n70)**
Yes	38 (25.85)	13 (61.90)	2 (66.67)	11 (32.35)	7 (46.67)
Life Difficulties:					
No	93 (62.42)	6 (27.27)	2 (50.00)	13 (32.50)	9 (56.25)
Yes	56 (37.58)	16 (72.73)	2 (50.00)	27 (67.50)	7 (43.75)
Childhood Adversity:					
No	101 (41.74)	12 (36.36)	3 (42.86)	7 (10.00)	11 (32.35)
Yes	141 (58.26)	21 (63.64)	4 (57.14)	63 (90.00)	23 (67.65)
	Median (IQR)	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***
Number of Childhood Adversity Factors	1 (0-2)	1 (0-2)	1 (0-1)	2 (1-3)	1 (0-3)

IQR = Interquartile range. Numbers in each group available in Table 6-5 and Table 6-6.

Table 6-8: Unadjusted odds ratios and 95% CIs for each baseline diagnosis compared with controls

	PMD (n72) vs. controls			SAD (n21) vs. controls			Schizophrenia (n218) vs. controls			Bipolar (n70) vs. controls		
	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)
Age	0.97	0.95-1.00	0.022	0.97	0.92-1.01	0.141	0.94	0.93-0.96	<0.001	0.93	0.91-0.96	<0.001
Study centre:												
Nottingham	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
London	1.14	0.69-1.89	0.613	1.96	0.79-4.84	0.146	2.72	1.91-3.87	<0.001	2.04	1.20-3.45	0.008
Gender:												
Female	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Male	1.44	0.87-2.40	0.156	2.35	0.95-5.80	0.065	2.59	1.83-3.67	<0.001	1.29	0.77-2.15	0.156
Ethnicity:												
White British	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
African-Caribbean	1.79	0.79-4.03	0.161	1.18	0.26-5.34	0.828	6.23	4.04-9.59	<0.001	4.29	2.12-8.66	<0.001
Black African	2.17	0.86-5.47	0.100	3.28	0.99-10.87	0.052	4.68	2.60-8.54	<0.001	4.68	2.04-10.74	<0.001
White Other	0.62	0.21-1.83	0.388	-	-	-	1.56	0.88-2.77	0.130	0.85	0.28-2.56	0.772
Asian (all)	5.70	1.95-16.66	0.001	2.15	0.25-18.45	0.485	3.72	1.42-9.75	0.008	6.69	2.16-20.75	0.001
Other	11.72	3.72-36.92	<0.001	-	-	-	6.54	2.21-19.41	0.001	14.28	4.36-46.78	<0.001
Place of birth:												
UK	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Non-UK	1.76	1.00-3.09	0.049	1.25	0.44-3.53	0.672	1.73	1.17-2.55	0.006	1.21	0.65-2.23	0.546
Relationship Status:												
Stable relationship	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Single	2.49	1.47-4.22	0.001	5.45	1.95-15.21	0.001	7.07	4.71-10.60	<0.001	3.06	1.80-5.22	<0.001
Ever had a long term relationship:												
Yes	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
No	2.21	1.23-3.97	0.008	2.53	0.93-6.87	0.068	6.18	4.08-9.36	<0.001	5.06	2.86-8.96	<0.001
Living with:												
With people	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Alone	1.39	0.82-2.39	0.228	3.34	1.37-8.17	0.008	2.24	1.58-3.18	<0.001	2.11	1.25-3.56	0.005
Level of Education:												
Higher	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-

	PMD (n72) vs. controls			SAD (n21) vs. controls			Schizophrenia (n218) vs. controls			Bipolar (n70) vs. controls		
	uOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Further	1.00	0.42-2.38	0.996	1.84	0.45-7.56	0.399	2.22	1.28-3.86	0.005	1.44	0.72-2.86	0.303
School	2.40	1.18-4.85	0.015	2.10	0.57-7.73	0.264	3.10	1.87-5.14	<0.001	1.00	0.52-1.95	0.994
Employment Status:												
Employed/ other	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Unemployed	1.58	0.94-2.64	0.081	2.77	1.08-7.11	0.034	3.09	2.16-4.42	<0.001	1.99	1.18-3.34	0.009
Ever worked												
Yes	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
No	1.70	0.34-8.39	0.516	3.02	0.35-26.11	0.314	4.12	1.59-10.70	0.004	3.40	0.96-11.98	0.057
Contact with friends:												
Daily – monthly	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Never / less than monthly	4.60	1.98-10.69	<0.001	3.51	0.72-17.11	0.120	10.68	5.85-19.49	<0.001	2.94	1.16-7.46	0.023
Contact with family:												
Daily – monthly	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Never / less than monthly	2.99	0.88-10.14	0.079	9.34	2.23-39.17	0.002	2.41	0.90-6.43	0.079	1.41	0.29-6.74	0.667
Close confidants:												
Yes	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
No	4.73	2.32-9.67	<0.001	5.55	1.62-19.00	0.006	12.39	7.42-20.71	<0.001	4.73	2.32-9.67	<0.001
Family history of any mental illness:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	5.14	2.58-10.22	<0.001	8.67	3.06-24.60	<0.001	7.74	4.62-12.97	<0.001	9.38	4.89-17.99	<0.001
Family history of psychosis:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	5.70	2.37-13.71	<0.001	11.41	3.50-37.15	<0.001	12.98	6.75-24.97	<0.001	7.91	3.45-18.10	<0.001
Parental history of any mental illness:												

	PMD (n72) vs. controls			SAD (n21) vs. controls			Schizophrenia (n218) vs. controls			Bipolar (n70) vs. controls		
	uOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	6.61	2.54-17.20	<0.001	7.71	1.90-31.33	0.004	9.96	4.69-21.15	<0.001	10.39	4.27-25.29	<0.001
Parental history of psychosis:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	7.34	2.24-23.99	0.001	8.48	1.56-46.12	0.013	14.13	5.56-35.90	<0.001	8.73	2.77-27.46	<0.001
Life Events												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	4.57	1.75-11.92	0.002	5.62	0.49-64.18	0.165	1.34	0.60-3.03	0.475	2.46	0.83-7.27	0.104
Life Difficulties:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	4.49	1.65-12.20	0.003	1.68	0.23-12.36	0.608	3.50	1.66-7.36	0.001	1.31	0.46-3.73	0.613
Childhood Adversity:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	1.31	0.61-2.79	0.489	1.00	0.22-4.56	0.995	6.72	2.94-15.33	<0.001	1.56	0.73-3.36	0.255
Number of Childhood Adversity Factors	1.08	0.83-1.40	0.587	0.58	0.36-0.93	0.024	1.26	1.10-1.45	0.001	1.14	0.92-1.41	0.230

uOR = unadjusted odds ratio; CI = confidence intervals; OR calculated using weighted data.

The unadjusted analyses showed strong evidence that the following factors were associated with an increased odds of receiving a baseline diagnosis of PMD compared with being a control: being Asian (OR 5.70, 95% CI 1.95-16.66, p=0.001) or 'other' ethnicity (OR 11.72, 95% CI 3.72-36.92, p<0.001); being single (OR 2.49, 95% CI 1.47-4.22, p=0.001); never having had a long term relationship (OR 2.21, 95% CI 1.23-3.97, p=0.008); having contact with friends less than monthly (OR 4.60, 95% CI 1.98-10.69, p<0.001); having no close confidants (OR 4.73, 95% CI 2.32-9.67, p<0.001); having a family history of mental illness (OR 5.14, 95% CI 2.58-10.22, p<0.001), family history of psychosis (OR 5.70, 95% CI 2.37-13.71, p<0.001), parental history of mental illness (OR 6.61, 95% CI 2.54-17.20, p<0.001), or parental history of psychosis (OR 7.34, 95% CI 2.24-23.99, p=0.001); having a severe life event during the year before onset of illness (OR 4.57, 95% CI 1.75-11.92, p=0.002); or having a severe life difficulty in the year before onset of illness (OR 4.49, 95% CI 1.65-12.20, p=0.003). There was moderate evidence that the following factors were associated with an increased odds of receiving a baseline diagnosis of PMD compared with being a control: lower age (OR 0.97, 95% CI 0.95-1.00, p=0.022); not having been born in the UK (OR 1.76, 95% CI 1.00-3.09, p=0.049); having school as the highest education level (OR 2.40, 95% CI 1.18-4.85, p=0.015). There was some weak evidence that the following factors were associated with an increased odds of receiving a baseline diagnosis of PMD compared with being a control: being unemployed (OR 1.58, 95% CI 0.94-2.64, p=0.081); and having contact with family less than monthly (OR 2.99, 95% CI 0.88-10.14, p=0.079). Interestingly, there was no evidence that childhood adversity was associated with an increased odds of receiving a baseline diagnosis of PMD (OR 1.31, 95% CI 0.61-2.79, p=0.489).

The unadjusted analyses showed strong evidence that the following factors were associated with an increased odds of receiving a baseline diagnosis of SAD compared with being a control: being single (OR 5.45, 95% CI 1.95-15.21, p=0.001); living alone (OR 3.34, 95% CI 1.37-8.17, p=0.008); having contact with family less than monthly (OR 9.34, 95% CI 2.23-39.17, p=0.002); having no close confidants (OR 5.55, 95% CI 1.62-19.00, p=0.006); and a having a family history of mental illness (OR 8.67, 95% CI 3.06-24.60, p<0.001), family history of psychosis (OR 11.41, 95% CI 3.50-37.15, p<0.001), parental history of mental illness (OR 7.71, 95% CI 1.90-31.33, p=0.004), parental history of psychosis (OR 8.48, 95% CI 1.56-46.12, p=0.013). There was moderate evidence that the being unemployed was associated with an increased odds of receiving a baseline diagnosis of SAD compared with being a control (OR 2.77, 95% CI 1.08-7.11, p=0.034). There was some weak evidence that the following factors were associated with increased odds of receiving a baseline diagnosis of SAD: being male (OR 2.35, 95% CI 0.95-5.80, p=0.065); being Black African (OR 3.28, 95% CI 0.99-10.87, p=0.052); and never having had a long term relationship (OR 2.53, 95% CI 0.93-6.87, p=0.068). Table 6-8 also indicates that having experienced more types of childhood adversity was associated with a reduced odds of SAD (OR 0.58, 95% CI 0.36-0.93, p=0.024). However, this is highly likely to be a spurious finding due to the very small number of cases (n7) available for the analysis due to missing data. The small numbers included in the analysis (and therefore low power) are also the likely cause for the finding that several factors which were not statistically significant at p < 0.1 but had ORs which were comparable or more extreme than in other diagnostic groups which did achieve statistical significance at the p<0.1 level. These factors were: lower age; never having worked; contact with friends less than monthly; and experiencing a life event during the year before onset of illness.

There was evidence (to varying degrees) that all factors investigated were associated with an increased odds of receiving a baseline diagnosis of schizophrenia except being white non-British and experiencing a life event during the year before onset of illness. Similarly, for cases with bipolar disorder, most factors were associated with an increased odds of receiving a diagnosis of bipolar disorder except gender, being white non-British, place of birth, level of education, contact with family, childhood adversity and experiencing a life event or life difficulty during the year before onset of illness.

6.3.2. Adjusted analyses

As might be expected, the numbers for the SAD group were very low. Therefore, it was not appropriate to use the data from this group in an adjusted model. For the other three diagnostic groups, the above regression analyses were run again but this time adjusting for four key variables; age, gender, centre and ethnicity (see Appendix O for adjusted results).

The differences that arise once gender, age, centre and ethnicity are controlled for is that there is now evidence that being single is associated with an increased odds of receiving a baseline diagnosis of PMD compared with being a control (OR 2.05, 95% CI 1.19-3.53, p=0.009), and the following factors are no longer associated with an increased odds of receiving a baseline diagnosis of PMD compared with being a control: never having had a long term relationship (OR 0.79, 95% CI 0.13-4.94, p=0.799); and not having been born in the UK (OR 1.20, 95% CI 0.53-2.72, p=0.667).

Once gender, age, centre and ethnicity had been controlled for, there was evidence (to varying degrees) that all risk factors except place of birth, ever worked, and life events were associated with an increased odd of receiving a diagnosis of schizophrenia

compared with being a control. For cases with bipolar disorder, the same factors that were associated with increased odds in the unadjusted analysis were significantly associated in the adjusted analyses: being single, never having had a long term relationship, living alone, being unemployed, having contact with friends less than monthly, having no close confidants and family or parental history of mental illness or psychosis. However, never having worked was no longer associated with a diagnosis of bipolar disorder, and having a life event in the year prior to onset became significantly associated with increased odds of bipolar disorder.

Both the adjusted and unadjusted analyses provided evidence that more of the psychosocial risk factors investigated in this thesis were associated with schizophrenia and bipolar disorder than PMD (and SAD within the unadjusted analyses only).

6.3.3. Exploratory analysis of life events based on baseline diagnosis

Exploratory analyses were conducted to investigate life events and difficulties. Results are presented in Table 6-9 and Table 6-10. Table 6-10 indicates that the odds of PMD cases having experienced both a life event and a life difficulty during the year prior to illness onset was around 5 times higher than for controls (OR 5.35, 95% CI 2.04-14.03, p=0.001), compared with only around 50% higher (OR 1.56, 95% CI 0.63-3.87, p=0.342) for schizophrenia cases and around 2 times higher (OR 1.94, 95% CI 0.56-6.74, p=0.294) for bipolar disorder cases. In contrast, the odds of schizophrenia cases having experienced either a life event *OR* a life difficulty during the year prior to illness onset was around 8 times higher than for controls (OR 8.54, 95% CI 2.85-25.56, p<0.001), compared with around 6 times higher (OR 6.83, 95% CI 1.92-24.29, p=0.003) for PMD cases and 2 times higher (OR 2.28, 95% CI 0.74-7.01, p=0.152) for bipolar disorder cases. However, these analyses are based on small sample sizes and must

therefore be interpreted with caution. The results based on the SAD group are based on a total of 3 cases and therefore no conclusions can be drawn from these findings.

As previous research has found that the humiliation/entrapment component of the LEDs is more highly associated with depression than other key components such as loss or danger,[438] an exploratory analysis examining humiliation and odds for PMD was performed. Table 6-11 contains the numbers for each diagnostic group for humiliation/entrapment events at different time points. Table 6-12 shows that there was evidence that independent humiliation difficulties of any type in the year pre onset were associated with an increased odds of a baseline diagnosis of PMD (OR 12.85, 95% CI 3.62-45.67, p<0.001), schizophrenia (OR 6.68, 95% CI 2.04-21.78, p=0.002) and bipolar disorder (OR 6.36, 95% CI 1.36-29.75, p=0.019), but PMD had the highest odds ratio (although there is a large amount of overlap and some of these confidence intervals are very wide indicating imprecise estimates of effects). There was strong evidence that PMD was associated with an increased odds of having experienced an independent humiliation or entrapment event at 4 weeks (OR 21.74, 95% CI 2.14-220.90, p=0.009), 3 months (OR 13.30, 95% CI 2.91-60.88, p=0.001), 6 months (OR 10.70, 95% CI 2.90-39.41, p<0.001) and 1 year (OR 5.81, 95% CI 1.81-18.63, p=0.003) prior to onset. There was no evidence for this association in bipolar disorder cases and only very weak evidence for this association at 3 and 6 months in schizophrenia cases. There was also evidence of a temporal relationship in the PMD cases, with higher odds ratios at time periods closer to onset. The results based on the SAD group are based on a total of 3 cases and therefore no conclusions can be drawn from these findings although they do follow the exact same pattern as the PMD group. Independent humiliation or entrapment severe events during the 1 week prior to onset were unable to be computed as no controls had this type of event in this time period.

Table 6-9: Life events and difficulties exploratory analysis based on baseline diagnosis

	Control	PMD	SAD	Schizophrenia	Bipolar
	N (%)	*N (%)*	*N (%)*	*N (%)*	*N (%)*
Life Event in the last year:					
No	109 (74.15)	8 (38.10)	1 (33.33)	23 (67.65)	8 (53.33)
Yes	38 (25.85)	13 (61.90)	2 (66.66)	11 (32.35)	7 (46.67)
Life Difficulty in the last year					
No	93 (62.58)	6 (27.27)	2 (50.00)	13 (32.50)	9 (56.25)
Yes	56 (37.58)	16 (72.73)	2 (50.00)	27 (67.50)	7 (43.75)
Life Event or difficulty in the last year					
No	79 (53.38)	3 (14.29)	1 (33.33)	4 (11.76)	5 (33.33)
Yes	69 (46.62)	18 (85.71)	2 (66.67)	30 (88.24)	10 (66.67)
Life Event and difficulty in the last year					
No	121 (82.88)	10 (47.62)	1 (33.33)	25 (75.76)	10 (71.43)
Yes	25 (17.12)	11 (52.38)	2 (66.67)	8 (24.24)	4 (28.57)

Table 6-10: Unadjusted odds ratios and 95% CIs for the life events and difficulties exploratory analysis based on baseline diagnosis

	PMD (n21) vs. controls			SAD (n3) vs. controls			Schizophrenia (n33) vs. controls			Bipolar (n14) vs. controls		
	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)
Life Events:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	4.57	1.75-11.92	0.002	5.62	0.49-64.18	0.165	1.34	0.60-3.03	0.475	2.46	0.83-7.27	0.104
Life Difficulties:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	4.49	1.65-12.20	0.003	1.68	0.23-12.36	0.608	3.50	1.66-7.36	0.001	1.31	0.46-3.73	0.613
Life Events or Life difficulty:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	6.83	1.92-24.29	0.003	2.28	0.20-25.82	0.507	8.54	2.85-25.56	<0.001	2.28	0.74-7.01	0.152
Life Events and Life difficulty:												
No	1.0	-	-	1.0	-	-	1.0	-	-	1.0	-	-
Yes	5.35	2.04-14.03	0.001	9.72	0.84-112.23	0.068	1.56	0.63-3.87	0.342	1.94	0.56-6.74	0.294

uOR = unadjusted odds ratio; CI = confidence intervals; OR calculated using weighted data.

Table 6-11: Humiliation exploratory analysis based on baseline diagnosis

	Control	**PMD**	**SAD**	**Schizophrenia**	**Bipolar**
	N (%)	***N (%)***	***N (%)***	***N (%)***	***N (%)***
Severe humiliation difficulty of any type in the year pre onset					
No	145 (96.67)	15 (68.18)	2 (50.00)	33 (80.49)	13 (81.25)
Yes	5 (3.33)	7 (31.82)	2 (50.00)	8 (19.51)	3 (18.75)
Independent humiliation or entrapment severe event 1 week pre onset					
No	146 (100)	20 (90.91)	3 (100)	37 (94.87)	17 (100)
Yes	0 (0)	2 (9.09)	0 (0)	2 (5.13)	0 (0)
Independent humiliation or entrapment severe event 4 weeks pre onset					
No	145 (99.32)	19 (86.36)	3 (75.00)	37 (97.37)	16 (94.12)
Yes	1 (0.68)	3 (13.64)	1 (25.00)	1 (2.63)	1 (5.88)
Independent humiliation or entrapment severe event 3 months pre onset					
No	143 (97.95)	17 (77.27)	2 (66.67)	33 (91.67)	16 (94.12)
Yes	3 (2.05)	5 (22.73)	1 (33.33)	3 (8.33)	1 (5.88)
Independent humiliation or entrapment severe event 6 months pre onset					
No	141 (96.58)	15 (71.43)	2 (66.67)	32 (88.89)	14 (87.50)
Yes	5 (3.42)	6 (28.57)	1 (33.33)	4 (11`.11)	2 (12.50)
Independent humiliation or entrapment severe event 12 months pre onset					
No	138 (93.88)	15 (71.43)	2 (66.67)	28 (84.85)	13 (86.67)
Yes	9 (6.12)	6 (28.57)	1 (33.33)	5 (15.15)	2 (13.33)

Table 6-12: Unadjusted odds ratios and 95% CIs for the humiliation exploratory analysis based on baseline diagnosis

	PMD (n72) vs. controls			SAD (n20) vs. controls			Schizophrenia (n214) vs. controls			Bipolar (n71) vs. controls		
	uOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Independent humiliation difficulty of any type in the year pre onset	12.85	3.62-45.67	<0.001	27.54	3.18-238.34	0.003	6.68	2.04-21.78	0.002	6.36	1.36-29.75	0.019
Any independent humiliation or entrapment severe event 1 week pre onset	Unable to compute as no controls had this type of event in this time period											
Any independent humiliation or entrapment severe event 4 weeks pre onset	21.74	2.14-220.90	0.009	45.9	2.27-926.66	0.013	3.72	0.23-61.30	0.358	8.61	0.51-145.24	0.135
Any independent humiliation or entrapment severe event 3 months pre onset	13.30	2.91-60.88	0.001	22.62	1.57-324.96	0.022	4.11	0.79-21.38	0.093	2.83	0.28-28.94	0.381
Any independent humiliation or entrapment severe event 6 months pre onset	10.70	2.90-39.41	<0.001	13.37	1.03-174.13	0.048	3.34	0.85-13.20	0.085	3.82	0.67-21.62	0.130
Any independent humiliation or entrapment severe event 12 months pre onset	5.81	1.81-18.63	0.003	7.26	0.60-88.40	0.120	2.59	0.81-8.35	0.110	2.23	0.43-11.50	0.336

uOR = unadjusted odds ratio; OR calculated using weighted data.

6.4. Diagnostic change

For the purpose of being able to examine social adversity risk factors based on lifetime diagnosis, diagnostic change will be described briefly here but is further detailed in chapter 7.

Table 6-13 shows the number of cases with each diagnosis at baseline and follow-up. As can be seen in the table, there are 21 less cases with PMD at follow-up compared with baseline and 2 less cases of SAD. Twenty-eight cases were unable to be given a lifetime diagnosis due to lack of information.

Table 6-13: Number of cases with each baseline and follow-up diagnosis

Diagnosis	Baseline n (%)	Follow-up n (%)
Schizophrenia	218 (43.17)	225 (47.17)
PMD	72 (14.26)	51 (10.69)
Bipolar disorder/mania	70 (13.86)	73 (15.30)
SAD	21 (4.16)	19 (3.98)
SABP/SAM	10 (1.98)	20 (4.19)
Other / Unspecified nonorganic disorder	36 (7.13)	29 (6.08)
Acute and transient psychosis	29 (5.74)	16 (3.35)
Drug / alcohol induced psychosis	26 (5.15)	34 (7.13)
Delusional disorder	22 (4.36)	8 (1.68)
Schizotypal disorder	1 (0.20)	1 (0.21)
Other disorder	-	1 (0.21)
No follow-up	-	28 (5.54)

6.5. Social adversity risk factors by lifetime diagnosis

6.5.1. Missing Data

Table 6-14 shows that there are no differences in missing data between the diagnostic groups in many of the variables examined. However, there was evidence of differences between different diagnostic groups in missing data in the following variables: lifetime relationship, contact with friends, contact with family, family mental health history, life

events and childhood adversity data (possible bias associated with this is considered in chapter 8).

Table 6-14: Missing data in the risk factor variables by diagnostic group (lifetime data)

	PMD (n51)	**SAD (n19)**	**Schizophrenia (n225)**	**Bipolar (n73)**		
	N (%)	**N (%)**	**N (%)**	**N (%)**	***Chi2, df***	***P value***
Age						
Present	51 (100)	19 (100)	225 (100)	73 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Study centre:						
Present	51 (100)	19 (100)	225 (100)	73 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Gender:						
Present	51 (100)	19 (100)	225 (100)	73 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Ethnicity:						
Present	51 (100)	19 (100)	225 (100)	73 (100)	-	-
Missing	0 (0)	0 (0)	0 (0)	0 (0)		
Place of birth:						
Present	51 (100)	19 (100)	220 (97.8)	72 (98.6)	1.682, 3	0.883 (fisher's exact)
Missing	0 (0)	0 (0)	5 (2.2)	1 (1.4)		
Living circumstances:						
Present	51 (100)	19 (100)	220 (97.8)	73 (100)	3.222, 3	0.547 (fisher's exact)
Missing	0 (0)	0 (0)	5 (2.2)	0 (0)		
Relationship Status:						
Present	50 (98.0)	19 (100)	212 (94.2)	73 (100)	6.506, 3	0.107 (fisher's exact)
Missing	1 (2.0)	0 (0)	13 (5.8)	0 (0)		
Ever relationship						
Present	42 (82.4)	13 (68.4)	155 (68.9)	60 (82.2)	7.565, 3	0.056
Missing	9 (17.6)	6 (31.6)	70 (31.1)	13 (17.8)		
Level of Education:						
Present	50 (98.0)	18 (94.7)	218 (96.9)	73 (100)	2.930, 3	0.258 (fisher's exact)
Missing	1 (2.0)	1 (5.3)	7 (3.1)	0 (0)		
Employment Status:						
Present	50 (98.0)	19 (100)	215 (95.6)	73 (100)	4.664, 3	0.271 (fisher's exact)
Missing	1 (2.0)	0 (0)	10 (4.4)	0 (0)		
Ever worked						
Present	42 (82.4)	14 (73.7)	158 (70.2)	59 (80.8)	5.303, 3	0.151 (fisher's exact)
Missing	9 (17.6)	5 (26.3)	67 (29.8)	14 (19.2)		
Contact with friends:						
Present	39 (76.5)	10 (52.6)	137 (60.9)	54 (74.0)	8.499, 3	0.037
Missing	12 (23.5)	9 (47.4)	88 (39.1)	19 (26.0)		
Contact with family:						
Present	40 (74.0)	11 (57.9)	140 (62.2)	56 (76.7)	9.179, 3	0.027
Missing	11 (26.0)	8 (42.1)	85 (37.8)	17 (23.3)		
Close confidants:						
Present	41 (80.4)	12 (63.2)	166 (73.8)	60 (82.2)	4.371, 3	0.226 (fisher's exact
Missing	10 (19.6)	7 (36.8)	59 (26.2)	13 (17.8)		

	PMD (n51)	**SAD (n19)**	**Schizophrenia (n225)**	**Bipolar (n73)**		
	N (%)	**N (%)**	**N (%)**	**N (%)**	***Chi2, df***	***P value***
Family history of any mental illness:						
Present	42 (82.4)	13 (68.4)	150 (66.7)	58 (79.5)	7.876, 3	0.049
Missing	9 (17.6)	6 (31.6)	75 (33.3)	15 (20.5)		
Family history of psychosis:						
Present	42 (82.4)	13 (68.4)	150 (66.7)	58 (79.5)	7.876, 3	0.049
Missing	9 (17.6)	6 (31.6)	75 (33.3)	15 (20.5)		
Parental history of any mental illness:						
Present	42 (82.4)	13 (68.4)	150 (66.7)	58 (79.5)	7.876, 3	0.049
Missing	9 (17.6)	6 (31.6)	75 (33.3)	15 (20.5)		
Parental history of psychosis:						
Present	42 (82.4)	13 (68.4)	150 (66.7)	58 (79.5)	7.876, 3	0.049
Missing	9 (17.6)	6 (31.6)	75 (33.3)	15 (20.5)		
Life Events:						
Present	13 (25.5)	2 (10.5)	34 (15.1)	21 (28.8)	9.010, 3	0.031 (fisher's exact)
Missing	38 (74.5)	17 (89.5)	191 (84.9)	52 (71.2)		
Life Difficulties:						
Present	13 (25.5)	2 (10.5)	41 (18.2)	21 (28.8)	5.591, 3	0.139 (fisher's exact)
Missing	38 (74.5)	17 (89.5)	184 (81.8)	52 (71.2)		
Childhood Adversity:						
Present	27 (52.9)	7 (36.8)	73 (32.4)	36 (49.3)	11.545, 3	0.009
Missing	24 (47.1)	12 (63.2)	152 (67.6)	37 (50.7)		
Number of Childhood Adversity Factors:						
Present	27 (52.9)	7 (36.8)	73 (32.4)	36 (49.3)	11.545, 3	0.009
Missing	24 (47.1)	12 (63.2)	152 (67.6)	37 (50.7)		

*: p<0.05; **: p<0.01; ***: p<0.001***

6.5.2. Unadjusted analyses

To test the hypothesis that psychosocial risk factors are associated with PMD and SAD, comparisons were made for each lifetime diagnostic group (PMD and SAD plus the comparison groups of schizophrenia and bipolar disorder) compared with controls. This is shown in Table 6-15 & Table 6-16.

Table 6-15: Summary of potential risk factors for controls and each lifetime diagnostic group

	Controls (n391)	**PMD (n51)**	**SAD (n19)**	**Schizophrenia (n225)**	**Bipolar (n73)**
	Median (IQR)	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***
Age	35 (28-47)	36 (30-46)	29 (22-41)	28 (22-35)	27 (23-33)
	N (%)	***N (%)***	***N (%)***	***N (%)***	***N (%)***
Study centre:					
Nottingham	208 (53.20)	29 (56.86)	9 (47.37)	70 (31.11)	30 (41.10)
London	183 (46.80)	22 (43.13)	10 (52.63)	155 (68.89)	43 (58.90)
Gender:					
Female	230 (58.82)	26 (50.98)	9 (47.37)	81 (36.00)	46 (63.01)
Male	161 (41.18)	25 (49.02)	10 (52.63)	144 (64.00)	27 (36.99)
Ethnicity:					
White British	241 (61.64)	31 (60.78)	12 (63.16)	87 (38.67)	33 (45.21)
African-Caribbean	74 (18.93)	6 (11.76)	4 (21.05)	66 (29.33)	17 (23.29)
Black African	21 (5.37)	3 (5.88)	2 (10.53)	34 (15.11)	9 (12.33)
White Other	42 (10.74)	3 (5.88)	1 (5.26)	18 (8.00)	4 (5.48)
Asian (all)	8 (2.05)	4 (7.84)	0 (0)	8 (3.56)	6 (8.22)
Other	5 (1.28)	4 (7.84)	0 (0)	12 (5.33)	4 (5.48)
Place of birth:					
UK	307 (78.52)	38 (74.51)	16 (84.21)	156 (70.91)	58 (80.56)
Non-UK	84 (21.48)	13 (25.49)	3 (15.79)	64 (29.09)	14 (19.44)
Relationship Status:					
Stable relationship	238 (60.87)	24 (48.00)	8 (42.11)	38 (17.92)	27 (36.99)
Single	153 (39.13)	26 (52.00)	11 (57.89)	174 (82.08)	46 (63.01)
Ever had a long term relationship:					
Yes	296 (76.68)	29 (69.05)	8 (61.54)	50 (32.26)	28 (46.67)
No	90 (23.32)	13 (30.95)	5 (38.46)	105 (67.74)	32 (53.33)
Living with:					
With people	270 (69.05)	27 (52.94)	12 (63.16)	106 (48.18)	49 (67.12)
Alone	121 (30.95)	24 (47.06)	7 (36.84)	114 (51.82)	24 (32.88)
Level of Education:					
Higher	95 (24.48)	6 (12.00)	3 (16.67)	22 (10.09)	17 (23.29)
Further	114 (29.38)	11 (22.00)	5 (27.78)	56 (25.69)	26 (35.62)
School	179 (46.13)	33 (66.00)	10 (55.56)	140 (64.22)	30 (41.10)
Employment Status:					
Employed and other	232 (59.34)	21 (42.00)	12 (63.16)	64 (29.77)	39 (53.42)
Unemployed	159 (40.66)	29 (58.00)	7 (36.84)	151 (70.23)	34 (46.58)
Ever worked					
Yes	383 (98.21)	42 (100.00)	13 (92.86)	143 (90.51)	56 (94.92)
No	7 (1.79)	0 (0)	1 (7.14)	15 (9.49)	3 (5.08)
Contact with friends:					
Daily – monthly	360 (95.24)	31 (79.49)	9 (90.00)	86 (62.77)	50 (92.59)
Never / less than monthly	18 (4.76)	8 (20.51)	1 (10.00)	51 (37.23)	4 (7.41)
Contact with family:					
Daily – monthly	359 (97.55)	38 (95.00)	11 (100)	126 (90.00)	55 (98.21)
Never / less than monthly	9 (2.45)	2 (5.00)	0 (0)	14 (10.00)	1 (1.79)
Close confidants:					
Yes	361 (93.04)	30 (73.17)	9 (75.00)	88 (53.01)	51 (85.00)
No	27 (6.96)	11 (26.83)	3 (25.00)	78 (46.99)	9 (15.00)
Family history of any mental illness:					
No	360 (92.07)	23 (54.76)	6 (46.15)	94 (62.67)	30 (51.72)
Yes	31 (7.93)	19 (45.24)	7 (53.85)	56 (37.33)	28 (48.28)
Family history of psychosis:					
No	375 (95.91)	29 (69.05)	8 (61.54)	104 (69.33)	44 (75.86)

	Controls (n391)	**PMD (n51)**	**SAD (n19)**	**Schizophrenia (n225)**	**Bipolar (n73)**
Yes	16 (4.09)	13 (30.95)	5 (38.46)	46 (30.67)	14 (24.14)
Parental history of any mental illness:					
No	380 (97.19)	32 (76.19)	10 (76.92)	120 (80.00)	41 (70.69)
Yes	11 (2.81)	10 (23.81)	3 (23.08)	30 (20.00)	17 (29.31)
Parental history of psychosis:					
No	384 (98.21)	35 (83.33)	10 (76.92)	125 (83.33)	48 (82.76)
Yes	7 (1.79)	7 (16.67)	3 (23.08)	25 (16.67)	10 (17.24)
Life Events					
No	109 (74.15)	6 (46.15)	2 (100)	21 (61.76)	9 (42.86)
Yes	38 (25.85)	7 (53.85)	0 (0)	13 (38.24)	12 (57.14)
Life Difficulties:					
No	93 (62.42)	4 (30.77)	2 (100)	13 (31.71)	7 (33.33)
Yes	56 (37.58)	9 (69.23)	0 (0)	28 (68.29)	14 (66.67)
Childhood Adversity:					
No	101 (41.74)	6 (22.22)	1 (14.29)	12 (16.44)	10 (27.78)
Yes	141 (58.26)	21 (77.78)	6 (85.71)	61 (83.56)	26 (72.22)
	Median (IQR)	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***	***Median (IQR)***
Number of Childhood Adversity Factors	1 (0-2)	1 (1-3)	1 (1-2)	2 (1-3)	n 1 (0-2.5)

IQR=Interquartile range. Numbers in each group reported in Table 6-14.

Table 6-16: Unadjusted odds ratios and 95% CIs for each lifetime diagnosis compared with controls

	PMD (n51) vs. controls			SAD (n19) vs. controls			Schizophrenia (n225) vs. controls			Bipolar (n73) vs. controls		
	uOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Age	1.00	0.98-1.03	0.693	0.95	0.91-0.99	0.011	0.94	0.92-0.95	<0.001	0.93	0.91-0.96	<0.001
Study centre:												
Nottingham	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
London	0.91	0.51-1.65	0.766	1.34	0.53-3.37	0.536	2.67	1.88-3.78	<0.001	1.73	1.04-2.88	0.036
Gender:												
Female	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Male	1.39	0.77-2.50	0.274	1.60	0.64-4.05	0.317	2.57	1.82-3.62	<0.001	0.85	0.50-1.42	0.532
Ethnicity:												
White British	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
African-Caribbean	1.60	0.64 - 4.01	0.315	2.76	0.86-8.84	0.088	6.27	4.11-9.57	<0.001	4.26	2.23-8.14	<0.001
Black African	1.11	0.31-3.94	0.871	1.91	0.40-9.13	0.416	4.49	2.47-8.15	<0.001	3.13	1.32-7.41	0.009
White Other	0.56	0.16-1.90	0.349	0.48	0.06-3.78	0.484	1.19	0.65-2.17	0.578	0.70	0.23-2.07	0.513
Asian (all)	3.89	1.10-13.67	0.034	-	-	-	2.77	1.01-7.61	0.048	5.48	1.79-16.79	0.003
Other	6.22	1.58-24.43	0.009	-	-	-	6.65	2.28-19.44	0.001	5.84	1.49-22.88	0.011
Place of birth:												
UK	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Non-UK	1.37	0.69-2.70	0.365	0.75	0.21-2.64	0.655	1.64	1.12-2.42	0.012	0.97	0.51-1.83	0.915
Relationship Status:												
Stable relationship	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Single	1.84	1.02-3.34	0.044	2.34	0.92-5.97	0.075	7.80	5.17-11.75	<0.001	2.90	1.72-4.88	<0.001
Ever had a long term relationship:												
Yes	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
No	1.62	0.80-3.27	0.176	2.26	0.72-7.11	0.163	7.59	5.00-11.54	<0.001	4.13	2.35-7.27	<0.001
Living with:												
With people	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Alone	2.23	1.23-4.04	0.008	1.46	0.56-3.82	0.437	2.70	1.90-3.82	<0.001	1.23	0.72-2.10	0.454
Level of Education:												
Higher	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Further	1.68	0.60-4.74	0.323	1.53	0.36-6.59	0.567	2.34	1.33-4.13	0.003	1.41	0.72-2.76	0.322

	PMD (n51) vs. controls			SAD (n19) vs. controls			Schizophrenia (n225) vs. controls			Bipolar (n73) vs. controls		
	uOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
School	3.15	1.27-7.81	0.013	1.91	0.51-7.12	0.335	3.65	2.17-6.12	<0.001	1.01	0.53-1.93	0.973
Employment Status:												
Employed /other	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Unemployed	2.06	1.13-3.75	0.018	0.87	0.33-2.26	0.775	3.52	2.46-5.04	<0.001	1.30	0.78-2.16	0.309
Ever worked												
Yes	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
No	>0.01	>0.01->0.01	<0.001	3.72	0.43-32.56	0.235	5.08	2.03-12.72	0.001	2.59	0.65-10.33	0.178
Contact with friends:												
Daily – monthly	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Never / less than monthly	4.98	1.99-12.46	0.001	2.15	0.26-17.94	0.481	11.45	6.31-20.78	<0.001	1.55	0.50-4.78	0.450
Contact with family:				Unable to compute as no SAD cases reported no contact / less than monthly contacts with family								
Daily – monthly	1.00	-	-				1.00	-	-	1.00	-	-
Never / less than monthly	1.97	0.41-9.49	0.399				4.15	1.74-9.91	0.001	0.68	0.08-5.49	0.717
Close confidants:												
Yes	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
No	5.09	2.28-11.36	<0.001	4.63	1.18-18.20	0.028	12.30	7.39-20.48	<0.001	2.45	1.08-5.55	0.032
Family history of any mental illness:												
No	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Yes	10.23	4.96-21.08	<0.001	14.45	4.53-46.06	<0.001	7.38	4.42-12.32	<0.001	11.56	6.05-22.08	<0.001
Family history of psychosis:												
No	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Yes	12.27	5.21-28.89	<0.001	17.11	4.92-59.53	<0.001	12.11	6.31-23.24	<0.001	8.71	3.85-19.71	<0.001
Parental history of any mental illness:												
No	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Yes	11.24	4.32-29.25	<0.001	10.79	2.56-45.60	0.001	9.00	4.23-19.13	<0.001	14.92	6.35-35.04	<0.001
Parental history of psychosis:												
No	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-

	PMD (n51) vs. controls			SAD (n19) vs. controls			Schizophrenia (n225) vs. controls			Bipolar (n73) vs. controls		
	uOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Yes	12.72	3.98-40.61	<0.001	19.07	4.11-88.53	<0.001	12.72	4.99-32.38	<0.001	13.25	4.52-38.78	<0.001
Life Events				Unable to compute as no SAD cases experienced a life event								
No	1.00	-	-				1.00	-	-	1.00	-	-
Yes	3.28	1.03-10.42	0.044				1.74	0.79-3.83	0.169	3.75	1.46-9.63	0.006
Life Difficulties:				Unable to compute as no SAD cases experienced life difficulties								
No	1.00	-	-				1.00	-	-	1.00	-	-
Yes	3.79	1.11-12.93	0.034				3.63	1.73-7.61	0.001	3.37	1.28-8.88	0.014
Childhood Adversity:												
No	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-
Yes	2.61	1.01-6.73	0.047	4.48	0.53-37.93	0.169	3.80	1.94-7.44	<0.001	1.94	0.89-4.22	0.094
Number of Childhood Adversity Factors	1.28	1.03-1.60	0.028	0.98	0.76-1.26	0.873	1.24	1.07-1.43	0.004	1.20	0.97-1.47	0.087

uOR = unadjusted odds ratio; CI = confidence intervals; OR calculated using weighted data.

The unadjusted analyses showed strong evidence that the following factors were associated with an increased odds of receiving a lifetime diagnosis of PMD compared with being a control: being of 'other' ethnicity (OR 6.22, 95% CI 1.58-24.43, p=0.009); living alone (OR 2.23, 95% CI 1.23-4.04, p=0.008); having contact with friends less than monthly (OR 4.87, 95% CI 1.99-12.46, p=0.001); having no close confidants (OR 5.09, 95% CI 2.28-11.36, p<0.001); and having a family history of mental illness (OR 10.23, 95% CI 4.96-21.08, p<0.001), family history of psychosis (OR 12.27, 95% CI 5.21-28.89, p<0.001), parental history of mental illness (OR 11.24, 95% CI 4.32-29.25, p<0.001), or parental history of psychosis (OR 12.72, 95% CI 3.98-40.61, p<0.001). There was strong evidence that having ever worked was associated with a reduced odds of PMD (OR >0.01, 95% CI >0.01 to >0.01, p<0.001). There was moderate evidence that the following factors were associated with an increased odds of receiving a lifetime diagnosis of PMD compared with being a control: being Asian (OR 3.89, 95% CI 1.10-13.67, p=0.034); being single (OR 1.48, 95% CI 1.02-3.34, p=0.044); having school as the highest education level (OR 3.15, 95% CI 1.27-7.81, p=0.013); being unemployed (OR 2.06, 95% CI 1.13-3.75, p=0.018); having a severe life event during the year before onset of illness (OR 3.28, 95% CI 1.03-10.42, p=0.044); having a severe life difficulty in the year before onset of illness (OR 3.79, 95% CI 1.11-12.93, p=0.034); and having experienced childhood adversity (OR 2.61, 95% CI 1.01-6.73, p=0.047). There was also moderate evidence that increasing numbers of types of childhood adversity was associated with increasing odds of PMD (OR 1.28, 95% CI 1.03-1.60, p=0.028).

The unadjusted analyses showed evidence that very few factors were associated with increased odds of receiving a lifetime diagnosis of SAD. However, there was strong evidence that the following were associated with a lifetime diagnosis of SAD: having a family history of mental illness (OR 14.45, 95% CI 4.53-46.06, p<0.001), family history

of psychosis (OR 17.11, 95% CI 4.92-59.53, p<0.001), parental history of mental illness (OR 10.79, 95% CI 2.56-45.60, p=0.001), or parental history of psychosis (OR 19.07, 95% CI 4.11-88.53, p<0.001). There was moderate evidence that the following were associated with increased odds of receiving a lifetime diagnosis of SAD: being younger (OR 0.95, 95% CI 0.91-0.99, p=0.011); and having no close confidants (OR 4.63, 95% CI 1.18-18.20, p=0.028). There was some weak evidence that being African Caribbean (OR 2.76, 95% CI 0.86-8.84, p=0.088) and being single (OR 2.34, 95% CI 0.92-5.97, p=0.075) was associated with an increased odds of receiving a lifetime diagnosis of SAD.

Within the analyses of SAD cases, there were several factors which were not statistically significant but for which ORs which were comparable or more extreme than in other diagnostic groups which were statistically significant. This is likely due to a power issue. These factors were: never having had a long term relationship; never having worked; contact with friends less than monthly; and having experienced childhood adversity. Contact with family, life events and life difficulties could not be calculated as no SAD cases reported less than monthly contacts with family, and none reported any life events or difficulties. The data on SAD cases is also based on extremely low numbers and therefore need to be interpreted with extreme caution.

There was evidence (to varying degrees) that all factors investigated were associated with an increased odds of receiving a lifetime diagnosis of schizophrenia being white non-British and experiencing a life event during the year before onset of illness. There was evidence (to varying degrees) that the following factors were associated with an increased odds of receiving a lifetime diagnosis of bipolar disorder: being younger; being from London; being Black African, African Caribbean, Asian or ‘other’ ethnicity;

being single; never having had a long term relationship; having no close confidants; having a family history or a parental history of mental illness or psychosis; having a severe life event during the year before onset of illness; having a severe life difficulty in the year before onset of illness; having experience childhood adversity; and an increasing number of types of childhood adversity.

Important differences but also important similarities were picked up between the baseline and lifetime unadjusted analyses. Both the analyses based on the baseline and based on the life time diagnoses found evidence (to varying degrees) that the following risk factors were associated with an increased odds of PMD compared with controls: being Asian or 'other' ethnicity; being single; having school as the highest level of education; being unemployed; having contact with friends less than monthly; having no close confidants; having a family or parental history of mental illness or psychosis; having experienced a life event in the year prior to onset; and having experienced a life difficulty. Differences between the analyses were that baseline analyses showed evidence that the following risk factors were associated with an increased odds of PMD compared with controls, but this was not supported by the life time diagnoses (i.e. the odds ratio moved closer to one and the p-value increased to over 0.1): being younger (OR 0.97 versus OR 1.00); having not been born in the UK (OR 1.76 versus OR 1.37); never having had a long term relationship (OR 2.21 versus OR 1.62); and having contact with family less than monthly (OR 2.99 versus OR 1.97). There were also differences between the analyses in that life time analyses showed evidence that the following risk factors were associated with an increased odds of PMD compared with controls, but this was not supported by the baseline diagnoses (i.e. in the baseline analyses, the odds ratio was closer to one and the p-value was over 0.1): living alone (OR 2.23 versus OR 1.39); having worked (never having worked OR >0.01 versus OR

1.70); having experienced childhood adversity (OR 2.61 versus OR 1.31); and having experienced an increasing number of different types of childhood adversity (OR 1.28 versus OR 1.08).

Both the unadjusted analyses based on the baseline and based on the lifetime diagnoses found evidence (to varying degrees) that the following risk factors were associated with an increased odds of SAD compared with controls: being single; having no close confidants; and having a family or parental history of mental illness or psychosis. Differences between the analyses were that baseline analyses showed evidence that the following risk factors were associated with an increased odds of SAD compared with controls, but this was not supported by the lifetime diagnoses (i.e. the odds ratio moved closer to one and the p-value increased to over 0.1): being male (OR 2.35 versus OR 1.60); being Black African (OR 3.28 versus OR 1.91); never having had a long term relationship (OR 2.52 versus OR 2.26); living alone (OR 3.34 versus OR 1.46); being unemployed (OR 2.77 versus OR 0.87). Differences between the analyses were that lifetime analyses showed evidence that the following risk factors were associated with an increased odds of SAD compared with controls, but this was not supported by the baseline diagnoses (i.e. in the baseline analyses, the odds ratio was closer to one and the p-value was over 0.1): being younger (OR 0.95 versus OR 0.97) and being African-Caribbean (OR 2.76 versus OR1.18).

6.5.3. Adjusted analyses

As in adjusted analyses based on the baseline diagnoses, the numbers in the SAD group were very low. Therefore, it is not appropriate to use the data from this group into an adjusted model. For the other three diagnostic groups, the above regression analyses

were run again but this time adjusting for four key variables; age, gender, centre and ethnicity (see Appendix O for adjusted analyses).

The only differences which arose between the adjusted and unadjusted analyses of risk factors in PMD cases was the degree of evidence that was detected, i.e. the evidence for some variables got slightly less and for others slightly more.

Once gender, age, centre and ethnicity were controlled for, there was evidence (to varying degrees) that all risk factors except place of birth and ever worked were significantly associated with an increased odds of receiving a lifetime diagnosis of schizophrenia. The confidence interval and p-values were not able to be calculated for life difficulties data due to the numbers being so low so although the odds ratio is fairly high (3.36), no conclusions can be reached about this data. For cases with bipolar disorder, there was evidence that mostly the same factors that were associated with an increased odds in the unadjusted analysis were significantly associated in the adjusted analyses: being single, never having had a long term relationship, having no close confidants and family or parental history of mental illness or psychosis and experiencing a life event in the year pre onset. As with the other diagnoses, it was not possible to calculate the confidence intervals and p-values for life difficulties data due to the numbers being so low so although the odds ratio is fairly high (3.61), no conclusions can be reached about this data. After adjusting for gender, age, centre and ethnicity, evidence became stronger for an association with employment status (OR 1.58, 95% CI 0.94-2.64, p=0.082), but weaker for childhood adversity (OR 1.55, 95% CI 0.65-3.71, p=0.323) and the number of different types of childhood adversities (OR 1.15, 95% CI 0.91-1.46, p=0.241).

As with the baseline diagnosis analyses, both the adjusted and unadjusted analyses provided evidence that more of the psychosocial risk factors investigated in this thesis were associated with schizophrenia and bipolar disorder than PMD (and SAD within the unadjusted analyses only).

Important differences but also important similarities were picked up between the baseline and lifetime adjusted analyses. Both the adjusted analyses based on the baseline and based on the life time diagnoses found evidence (to varying degrees) that the following risk factors were associated with an increased odds of PMD compared with controls: being single; having school as the highest level of education; being unemployed; having contact with friends less than monthly; having no close confidants; having a family or parental history of mental illness or psychosis; and having experienced a life event in the year prior to onset. In both the baseline diagnosis and lifetime diagnosis analyses, the effect size of the association between PMD and life difficulties was 2.71 or over. However, in the lifetime diagnosis analyses, the uncertainty surrounding the estimate was unable to be calculated. There were some differences between the baseline and lifetime diagnosis analyses. The baseline analyses showed evidence that the following risk factors were associated with an increased odds of PMD compared with controls, but this was not supported by the life time diagnoses (i.e. the odds ratio moved closer to one and the p-value increased to over 0.1): having contact with family less than monthly (OR 3.15 versus OR 1.83). There were also differences between the analyses in that life time analyses showed evidence that the following risk factors were associated with an increased odds of PMD compared with controls, but this was not supported by the baseline diagnoses (i.e. in the baseline analyses, the odds ratio was closer to one and the p-value was over 0.1): living alone (OR 2.26 versus OR 1.41); having worked (never having worked OR <0.01versus OR

0.79); having experienced childhood adversity (OR 2.57 versus OR 1.30); and having experienced an increasing number of different types of childhood adversity (OR 1.26 versus OR 1.07).

6.5.4. Exploratory analysis of life events based on lifetime diagnosis

Exploratory analyses based on lifetime diagnoses were conducted to investigate life events and life difficulties. Results are presented in Table 6-17 and Table 6-18. Table 6-18 reveals that the odds of PMD cases having experienced both a life event and a life difficulty during the year prior to illness onset was 4.17 (95% CI 1.28-13.54, p=0.018) times the odds of controls, compared with only 2.11 (95% CI 0.89-5.02, p=0.09) for schizophrenia cases and 3.98 (95% CI 1.48-10.67, p=0.006) for bipolar disorder cases. On the other hand, the odds of schizophrenia cases having experienced either a life event or a life difficulty was 11.76 (95% CI 3.43-40.35, p<0.001) the odds of controls, compared with 3.79 (95% CI 1.00-14.41, p=0.050) for PMD cases and 4.84 (95% CI 1.55-15.13, p=0.007) for bipolar disorder cases. The results for the SAD group were based on a total of 2 cases neither of whom experienced a life event or difficulty and so the ORs could not be calculated. Therefore no conclusions can be drawn on the SAD cases.

An exploratory analysis examining humiliation/entrapment and odds for PMD using lifetime diagnosis was performed. Table 6-19 contains the numbers for each diagnostic group for humiliation/entrapment events at different time points.

Table 6-20 shows that independent humiliation difficulties of any type in the year pre onset were significantly associated with a diagnosis of PMD (OR 12.24, 95% CI 2.78-53.80, p=0.001), schizophrenia (OR 6.48, 95% CI 1.99-21.10, p=0.002) and bipolar disorder (OR 8.61, 95% CI 2.24-33.07, p=0.002), with PMD having the highest OR. There was strong evidence that having experienced an independent humiliation or entrapment event at 4 weeks (OR 25.00, 95% CI 2.09-299.00, p=0.011), 3 months (OR 20.10, 95% CI 3.88-104.24, p<0.001), 6 months (OR 11.88, 95% CI 2.70-52.27, p=0.001) and 1 year prior to onset (OR 6.45, 95% CI 1.65-25.16, p=0.007) was associated with an increased odds of PMD compared with controls.

Within the exploratory analysis of life events and difficulties, plus in the humiliation events exploratory analyses, there are also some interesting similarities and differences in the baseline and lifetime diagnosis analyses. Schizophrenia has the highest odds ratio for having experienced a life event *OR* difficulty in both analyses but the effect is still present in PMD cases. However, this difference is magnified in the lifetime diagnoses with the effect size getting larger for schizophrenia cases and lower for PMD cases in the life time diagnoses. PMD cases have the highest odds ratio for having experienced a life event *AND* difficulty in both analyse. Although this is non-significant in schizophrenia cases in the baseline analyses, it does reach significance in the life time diagnoses. For bipolar cases, there is no evidence of an increased odds ratio of having experienced a life event *OR* a life difficulty, or a life event *AND* life difficulty when based on the baseline diagnoses, but there is evidence of an increased odds ratio for both these items when based on the lifetime diagnoses.

As for the analyses on humiliation life events and life difficulties, the baseline and lifetime analyses both find evidence that independent humiliation difficulties are associated with an increased odds ratio for all the diagnoses (except SAD cannot be estimated in the lifetime analyses due to low numbers). Both the baseline and lifetime analyses find evidence that independent humiliation or entrapment events at 4 weeks, 3 months, 6 months and 12 months are associated with an increased odds of PMD compared with controls, and there is evidence of a temporal effect in both analyses with the effect getting stronger, the closer to onset. Both the baseline and the lifetime diagnosis analyses find some weak evidence that independent humiliation or entrapment events at certain points are associated with an increased odds of schizophrenia compared with controls. The baseline analyses reveal no association between independent humiliation or entrapment events and bipolar disorder. However, the lifetime diagnosis analyses reveal evidence that independent humiliation or entrapment events at 4 weeks, 3 months, 6 months and 12 months are associated with an increased odds of bipolar disorder, although with lesser effect sizes compared with PMD and without as strong evidence of a temporal effect.

There was moderate to strong evidence of the same in the bipolar disorder group (4 weeks: OR 13.75, 95% CI 1.19-159.27, p=0.036, 3 months: OR 7.14, 95% CI 1.34-38.12, p=0.021, 6 months: OR 10.03, 95% CI 2.74-36.72, p<0.001 and 1 year: OR 5.81, 95% CI 1.81-18.63, p=0.003). There was only moderate to weak evidence in the schizophrenia group that having experienced an independent humiliation or entrapment event at 4 weeks (OR 11.46, 95% CI 1.15-113.82, p=0.037), 3 months (OR 4.11, 95% CI 0.79-21.39, p=0.093), and 6 months (OR 3.45, 95% CI 0.87-13.64, p=0.077).

There was also evidence of a temporal relationship in having experienced an independent humiliation or entrapment event in PMD cases, with a higher OR at time periods closer to onset. It was not possible to compute the OR for the SAD group as no SAD cases experienced life events or difficulties.

Table 6-17: Life events and difficulties exploratory analysis based on lifetime diagnosis

	Control	PMD	SAD	Schizophrenia	Bipolar
	N (%)	*N (%)*	*N (%)*	*N (%)*	*N (%)*
Life Event in the last year:					
No	109 (74.15)	6 (46.15)	2 (100)	21 (61.76)	9 (42.86)
Yes	38 (25.85)	7 (53.85)	0 (0)	13 (38.24)	12 (57.14)
Life Difficulty in the last year					
No	93 (62.42)	4 (30.77)	2 (100)	13 (31.71)	7 (33.33)
Yes	56 (37.58)	9 (69.23)	0 (0)	28 (68.29)	14 (66.67)
Life Event or difficulty in the last year					
No	79 (53.38)	3 (23.08)	2 (100)	3 (8.82)	4 (19.05)
Yes	69 (46.62)	10 (76.92)	0 (0)	31 (91.18)	17 (80.95)
Life Event and difficulty in the last year					
No	121 (82.88)	7 (53.85)	2 (100)	23 (69.70)	11 (55.00)
Yes	25 (17.12)	6 (46.15)	0 (0)	10 (30.30)	9 (45.00)

Table 6-18: Unadjusted odds ratios and 95% CIs for the life events and difficulties exploratory analysis based on lifetime diagnosis

	PMD (n51) vs. controls			SAD (n19) vs. controls			Schizophrenia (n225) vs. controls			Bipolar (n73) vs. controls		
	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)	uOR (2dp)	95% CI (2dp)	P (3dp)
Life Events:				Unable to compute as no SAD cases experienced life events or difficulties								
No	1.00	-	-				1.00	-	-	1.00	-	-
Yes	3.28	1.03-10.42	0.044				1.74	0.79-3.83	0.169	3.75	1.46-9.63	0.006
Life Difficulties:				Unable to compute as no SAD cases experienced life events or difficulties								
No	1.00	-	-				1.00	-	-	1.00	-	-
Yes	3.79	1.11-12.93	0.034				3.63	1.73-7.61	0.001	3.37	1.28-8.88	0.014
Life Events or Life difficulty:				Unable to compute as no SAD cases experienced life events or difficulties								
No	1.00	-	-				1.00	-	-	1.00	-	-
Yes	3.79	1.00-14.41	0.050				11.76	3.43-40.35	<0.001	4.84	1.55-15.13	0.007
Life Events and Life difficulty:				Unable to compute as no SAD cases experienced life events or difficulties								
No	1.00	-	-				1.00	-	-	1.00	-	-
Yes	4.17	1.28-13.54	0.018				2.11	0.89-5.02	0.090	3.98	1.48-10.67	0.006

uOR = unadjusted odds ratio; CI = confidence intervals; OR calculated using weighted data.

Table 6-19: Humiliation exploratory analysis based on lifetime diagnosis

	Control	**PMD**	**SAD**	**Schizophrenia**	**Bipolar**
	N (%)	***N (%)***	***N (%)***	***N (%)***	***N (%)***
Severe humiliation difficulty of any type in the year pre onset					
No	145 (96.67)	9 (69.23)	2 (100)	34 (80.95)	16 (76.19)
Yes	5 (3.33)	4 (30.77)	0 (0)	8 (19.05)	5 (23.81)
Independent humiliation or entrapment severe event 1 week pre onset					
No	146 (100)	12 (92.31)	2 (66.67)	36 (94.74)	21 (95.45)
Yes	0 (0)	1 (7.69)	1 (33.33)	2 (5.26)	1 (4.55)
Independent humiliation or entrapment severe event 4 weeks pre onset					
No	145 (99.32)	11 (84.62)	2 (100)	36 (92.31)	20 (90.91)
Yes	1 (0.68)	2 (15.38)	0 (0)	3 (7.69)	2 (9.09)
Independent humiliation or entrapment severe event 3 months pre onset					
No	143 (97.95)	9 (69.23)	2 (100)	33 (91.67)	19 (86.36)
Yes	3 (2.05)	4 (30.77)	0 (0)	3 (8.33)	3 (13.64)
Independent humiliation or entrapment severe event 6 months pre onset					
No	141 (96.58)	9 (69.23)	2 (100)	31 (88.57)	16 (72.73)
Yes	5 (3.42)	4 (30.77)	0 (0)	4 (11.43)	6 (27.27)
Independent humiliation or entrapment severe event 12 months pre onset					
No	138 (93.88)	9 (69.23)	2 (100)	28 (84.85)	15 (71.43)
Yes	9 (6.12)	4 (30.77)	0 (0)	5 (15.15)	6 (28.57)

Table 6-20: Unadjusted odds ratios and 95% CIs for the humiliation exploratory analysis based on lifetime diagnosis

	PMD (n51) vs. controls			SAD (n19) vs. controls			Schizophrenia (n225) vs. controls			Bipolar (n73) vs. controls		
	uOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**uOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Independent humiliation difficulty of any type in the year pre onset	12.24	2.78-53.80	0.001	Unable to compute as no SAD cases experienced life events or difficulties			6.48	1.99-21.10	0.002	8.61	2.24-33.07	0.002
Any independent humiliation or entrapment severe event 1 week pre onset	Unable to compute as no controls had this type of event in this time period											
Any independent humiliation or entrapment severe event 4 weeks pre onset	25.00	2.09-299.00	0.011	Unable to compute as no SAD cases experienced life events or difficulties			11.46	1.15-113.82	0.037	13.75	1.19-159.27	0.036
Any independent humiliation or entrapment severe event 3 months pre onset	20.10	3.88-104.24	<0.001	Unable to compute as no SAD cases experienced life events or difficulties			4.11	0.79-21.39	0.093	7.14	1.34-38.12	0.021
Any independent humiliation or entrapment severe event 6 months pre onset	11.88	2.70-52.27	0.001	Unable to compute as no SAD cases experienced life events or difficulties			3.45	0.87-13.64	0.077	10.03	2.74-36.72	<0.001
Any independent humiliation or entrapment severe event 12 months pre onset	6.45	1.65-25.16	0.007	Unable to compute as no SAD cases experienced life events or difficulties			2.59	0.80-8.35	0.111	5.81	1.81-18.63	0.003

uOR = unadjusted odds ratio: CI = confidence intervals; OR calculated using weighted data.

CHAPTER 7. Results of clinical, social and service use outcomes 10 years after first episode of psychosis

"A person with psychotic depression suffers a dangerous combination of depressed mood and psychosis..."[161]

Rothschild (2009)

7.1. Aims of the chapter

This chapter aimed to describe and summarise the follow-up success for the entire incidence sample and to explore the clinical, social and service use outcomes of PMD and SAD cases compared with the other major psychotic diagnostic groups, schizophrenia and bipolar disorder. The importance of examining course of illness and outcome based on both baseline and lifetime diagnosis has already been discussed in chapter 4. Therefore, outcomes based on both baseline and lifetime diagnosis will be examined in section.

7.2. Sample

In the follow-up phase of the study, an attempt was made to trace all incidence cases identified in the case control study. As mentioned in Chapter 6, of the 511 cases included in the baseline analyses, six (1.2%) were excluded due to information that came to light after baseline that these patients either had an organic psychosis or were not first episode cases at baseline. Therefore, a total of 505 cases were included in the follow-up.

7.3. Follow-up description and exploration

7.3.1. Follow-up success

As well as using case notes to determine outcomes, every effort was made to follow cases up with an interview to ensure the maximum amount of information was gained. This is reflected in the fact that patients were located, contacted and interviewed all over the UK. There were also several patients who were traced to outside the UK and had

telephone interviews conducted. This included one case in Ireland, one in Norway and one in New Zealand.

7.3.2. Participant follow-up and functional outcomes

Follow-up data covering a ten year period (minimum 8 years, range of 8-13 years) was available for 379 (75.1%) cases. A further 33 (6.5%) cases were dead at follow-up and 26 (5.2%) were uncontactable as they had gone abroad (three cases had sufficient information at 8+ years although they were abroad when followed up at 10 years and are counted as followed up here). This left 67 cases (13.3%) who did not have a 10 year follow-up. As stated in the methods, cases were followed up using case notes which were supplemented with patient interview where possible. Table 7-1 gives the information on interview status. Twenty-one cases were traced to a current address but no contact with the participant was ever made and a further four were traced but they did not have sufficient capacity to consent to interview.

Table 7-1: Interview status at follow-up

Interview status	N (%)
Interviewed	208 (41.2)
Dead	33 (6.5)
Abroad	26 (5.2)
Refused interview	167 (33.1)
Traced, but no contact made	21 (4.2)
Traced, but no capacity	4 (0.8)
Not traced	46 (9.1)

*Cases who were abroad but were interviewed were counted as interviewed here

Table 7-2 presents the follow-up status of cases by baseline ICD-10 diagnosis. A chi-squared test showed that there was no difference in the follow-up status by diagnosis (Pearson Chi-Square 10.70, df12, p= 0.690 (fisher's exact)).

Table 7-2: Follow-up status by baseline ICD-10 diagnosis

	8-12 year follow-up	No follow-up	Dead	Aboard		
	N (%)	*N (%)*	*N (%)*	*N (%)*	*Chi^2 (df)*	*p value*
PMD	54 (75.0)	13 (18.1)	3 (4.2)	2 (2.8)	10.70 (2)	0.690 (fisher's exact)
SAD	18 (85.7)	3 (14.3)	0 (0)	0 (0)		
Schizophrenia	163 (74.8)	24 (11.0)	18 (8.3)	13 (6.0)		
Bipolar	53 (75.7)	8 (11.4)	3 (4.3)	6 (8.6)		
Other diagnoses	91 (73.4)	19 (15.3)	9 (7.3)	5 (4.0)		

df = degrees of freedom.

The median follow-up time for the cases who had 8+ years follow-up was 10.59 years (9.92-11.47 inter-quartile range). Table 7-3 presents the median follow-up time in years by diagnostic group for those with 8+ years follow-up. A Kruskal Wallis test revealed no significant differences between the groups (Chi2=4.765, df4, p=0.312).

Table 7-3: Follow-up time by diagnosis for those with 8+ years follow-up

Diagnosis	Median years follow-up time (IQR)	Range
PMD (n54)	10.59 (9.92-11.63)	8.08-13.13
SAD (n18)	10.66 (9.52-11.40)	8.42-13.62
Schizophrenia (n163)	10.52 (9.91 – 11.31)	8.32-13.38
Bipolar (n53)	10.55 (9.86-11.10)	8.35-13.37
Other diagnoses (n91)	10.89 (10.01-11.73)	8.18-13.70

IQR = Interquartile range.

7.3.3. Comparison of baseline variables for cases with follow-up data compared with those without follow-up data

Table 7-4 and Table 7-5 present the baseline demographic and clinical variables broken down by those with follow-up data compared with those without follow-up data; cases abroad and deceased cases are not included in these analyses.

Table 7-4 shows that there were no significant differences between those with and those without follow-up data at 8-12 years in terms of demographic variables (although level of qualification was on the cusp of being statistically significant at the traditional $p<0.05$ threshold with those with higher levels of education being less likely to be followed up).

Table 7-4: Comparison of baseline demographic variables of those with and those without follow-up data at 8 years+

	No follow-up at 8 years+ (n67)	**8-12 year follow-up (n379)**			
	Median (IQR)	***Median (IQR)***	***Wilcoxin z***	***df***	***P value***
Age	27.00 (20-33)	29.00 (22-36)	-1.842	-	0.066
	N (%)	***N (%)***	***Chi2***	***df***	***P value***
Study centre					
London	42 (62.7)	222 (58.6)	0.398	1	0.528
Nottingham	25 (37.3)	157 (41.4)			
Gender					
Male	42 (62.7)	211 (55.7)	1.141	1	0.285
Female	25 (37.3)	168 (44.3)			
Ethnicity					
White British	38 (56.7)	168 (44.3)	9.074	5	0.095 (fisher's exact)
Black Caribbean	12 (17.9)	97 (25.6)			
Black African	3 (4.5)	47 (12.4)			
White Other	6 (9.0)	25 (6.6)			
Asian	2 (3.0)	22 (5.8)			
Other (all)	6 (9.0)	20 (5.3)			
Place of birth					
UK	54 (80.6)	283 (75.9)	0.708	1	0.400
Non-UK	13 (19.4)	90 (24.1)			
Relationship Status					
Single	49 (75.4)	262 (72.8)	0.191	1	0.662
Steady relationship	16 (24.6)	98 (27.2)			
Living circumstances:					
Others	40 (59.7)	204 (54.6)	0.611	1	0.434
Alone	27 (40.3)	170 (45.5)			
Employment Status					
Unemployed	38 (58.5)	218 (58.5)	0.925	2	0.630
Economically inactive	9 (13.9)	67 (18.0)			
Employment	18 (27.7)	88 (23.6)			
Level of Education					
No qualifications	26 (40.6)	128 (34.9)	7.830	3	0.050
GCSE	14 (21.9)	93 (25.3)			
Further	10 (15.6)	102 (27.8)			
Higher	14 (21.9)	44 (12.0)			

IQR = Interquartile range. df = degrees of freedom.

Table 7-5: Comparison of baseline clinical variables of those with and those without follow-up data

	No follow-up (n67)	**8-12 year follow-up (n379)**			
	Median (IQR)	***Median (IQR)***	***Kruskal Wallis***	***df***	***P value***
DUP in days	53.50 (14.00-215.00)	60.00 (15.00-225.00)	-0.224	-	0.823
Age of onset	26.00 (19.00-33.00)	28.00 (22.00-34.00)	-1.639	-	0.101
	N (%)	***N (%)***	***Chi2***	***df***	***P value***
Diagnosis: PMD SAD Schizophrenia Bipolar Other psychoses	 13 (19.40) 3 (4.48) 24 (35.82) 8 (11.94) 19 (28.36)	 54 (14.25) 18 (4.75) 163 (43.01) 53 (13.98) 91 (24.01)	2.238	4	0.661 (fisher' s exact)
Mode of Onset: Sudden Precipitous Acute, no previous symptoms Acute, with previous symptoms Insidious No clear line of demarcation	 11 (18.3) 5 (8.3) 7 (11.7) 14 (23.3) 23 (38.3) 0 (0.0)	 45 (13.4) 19 (5.7) 46 (13.7) 42 (12.5) 170 (50.8) 13 (3.9)	9.734	5	0.082 (fisher' s exact)
Source of Referral: GP Emergency clinic/psychiatrist A&E Police/Prison/Courts Other	 21 (31.3) 10 (14.9) 16 (23.9) 12 (17.9) 8 (11.9)	 141 (38.1) 52 (14.1) 73 (19.7) 78 (21.1) 26 (7.0)	3.248	4	0.517
Initial Mode of Contact: Community Patient Voluntary Inpatient Compulsory Inpatient	 23 (34.3) 25 (37.3) 19 (28.4)	 120 (32.2) 118 (31.6) 135 (36.2)	1.641	2	0.440

IQR = Interquartile range.

Table 7-5 shows that those not followed up were no different clinically compared with those who were followed up including by diagnosis.

7.3.4. Core analytic sample

As stated in chapter 4, the purpose of this chapter was to compare outcomes in PMD and SAD cases to schizophrenia and bipolar cases. Hence, cases with other diagnoses were excluded from the analyses. Therefore, the analyses based on baseline diagnoses were based on a core analytic sample of the 381 cases (PMD, SAD, schizophrenia and bipolar cases only). Although 288 cases in this core analytic sample had 8-12 year

follow-up information, some cases who had died or were abroad had relevant information and could be included in some analyses. Furthermore, some cases who had 8-12 year follow-up information had some missing data. Therefore, each section will have a note about the number of cases in each particular analysis.

The analyses based on lifetime diagnoses were based on a core analytic sample of 368 cases (PMD, SAD, schizophrenia and bipolar cases only). As with the baseline core analytic sample, although 298 cases in this core analytic sample had 8-12 year follow-up information, some cases have some missing variables within this, and some cases who had died or were abroad were able to be included in some analyses. Therefore, each section will have a note about the number of cases in each particular analysis.

7.4. Diagnostic change

Although PMD, SAD, schizophrenia and bipolar disorder cases are the main diagnoses of interest in this thesis, all diagnoses will be included in this section on diagnostic change as change can involve all diagnoses. This section aimed to test the hypothesis that PMD and SAD cases would have a lower prospective consistency and higher retrospective consistency compared with schizophrenia and bipolar disorder.

7.4.1. Description

A lifetime diagnosis was made for each case if there was sufficient information to do so regardless of follow-up status (i.e. even if cases were deceased). A lifetime diagnosis was available for 477 out of 511 baseline cases. Twenty-eight cases had insufficient information to make a follow-up diagnosis. There was insufficient information to give a follow-up diagnosis for 5 (7.5%) baseline PMD cases, 3 (16.7%) SAD cases, 11 (5.3%)

schizophrenia cases, 4 (6.1%) bipolar disorder cases and 5 (4.2%) other diagnosis cases. Of the 6 excluded cases, 3 had a baseline diagnosis of schizophrenia and 3 had an 'other' diagnosis. A chi-squared analysis to test whether there was a difference between the diagnostic groups in those missing follow-up diagnosis showed that there was no evidence of a difference (chi2=3.982, df4, p=0.367 (fisher's exact)).

Table 7-6 presents a diagnosis movement matrix (baseline diagnosis by follow-up diagnosis) for those with a lifetime diagnosis.

Table 7-6: Baseline diagnosis by lifetime diagnosis

		Lifetime diagnosis (n477)				
		PMD (n51)	**SAD (n19)**	**Schizophrenia (n225)**	**Bipolar (n73)**	**Other (n109)**
Baseline diagnosis (n477)	**PMD (n67)**	33	2	16	7	9
	SAD (n18)	1	7	7	1	2
	Schizophrenia (n207)	8	6	157	8	28
	Bipolar (n66)	2	0	3	51	10
	Other (n119)	7	4	42	6	60

Table 7-6 shows that only 33/67 (49%) of PMD patients had the same lifetime diagnosis that they had at baseline. The majority of changers moved to schizophrenia (n16, 47%) with smaller numbers moving to 'other' diagnoses (psychosis not otherwise specified (n3, 9%), delusional disorder (n2, 6%), acute and transient psychoses (n1, 3%), drug induced psychosis (n1, 3%), schizoaffective bipolar disorder (n1, 3%)); and other disorder (n1, 3%), bipolar disorder (n7, 21%) and SAD (n2, 6%). Only 7/18 (39%) of SAD cases had the same lifetime diagnosis that they had at baseline, with a higher percentage of changers moving to a diagnosis of schizophrenia (n7, 64%) and the rest moving to PMD (n1, 9%), bipolar disorder (n1, 9%) and other diagnoses (psychosis not otherwise specified (n2, 18%)).

In terms of movement to a particular diagnosis, 18 cases moved from a non-PMD diagnosis at baseline to a lifetime diagnosis of PMD. Twelve cases moved from a non-SAD diagnosis at baseline to a lifetime diagnosis of SAD.

7.4.2. Calculation of prospective consistency for all groups

Prospective consistency is defined as the proportion of cases who have the same diagnosis at follow-up as they did at baseline. Table 7-7 presents the prospective consistency for each diagnostic group and shows that PMD and SAD both had low prospective consistencies of less than 50%. This is compared with a prospective consistency of 76% and 77% for schizophrenia and bipolar disorder respectively.

Table 7-7: Prospective consistency by diagnosis

Baseline diagnosis	Prospective consistency
PMD	49.3%
SAD	38.9%
Schizophrenia	75.9%
Bipolar	77.3%
Other	50.4%

Table 7-8 shows the odds ratios, confidence intervals and p values for the proportion of cases who have the same diagnosis at follow-up as they did at baseline (prospective validity). The table shows strong evidence that PMD cases were less likely to have the same diagnosis at follow-up as they did at baseline compared with schizophrenia cases (OR 0.31, 95% CI 0.17-0.55, $p<0.001$) and compared with bipolar cases (OR 0.29, 95% CI 0.13-0.60, $p=0.001$). There was evidence that SAD cases were less likely to have the same diagnosis at follow-up as they did at baseline compared with schizophrenia cases (OR 0.20, 95% CI 0.07-0.55, $p=0.002$) and compared with bipolar cases (OR 0.19, 95% CI 0.06-0.57, $p=0.003$).

Table 7-8: Odds ratios, confidence intervals and p values for the proportion of cases who have the same diagnosis at follow-up as they did at baseline (prospective consistency)

	PMD vs. SZ (n274)	PMD vs. BP (n133)	PMD vs. SAD (n85)	SAD vs. SZ (n225)	SAD vs. BP (n84)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Prospective consistency	0.31 (0.17-0.55)***	0.29 (0.13-0.60)***	1.53 (0.53-4.41)	0.20 (0.07-0.55)***	0.19 (0.06-0.57)***

* p<0.1; ** p<0.05; *** p<0.01; CI = 95% confidence interval.

7.4.3. Calculation of retrospective consistency for all groups

Retrospective consistently is defined as the proportion of cases who have the same diagnosis at baseline as they do at follow-up. Table 7-9 presents the retrospective consistency for each diagnostic group and shows that the retrospective consistency of PMD was similar to that of schizophrenia and bipolar disorder, 65-70%. The retrospective consistency for SAD was very low at 37%.

Table 7-9: Retrospective consistency by diagnosis

Lifetime diagnosis	Retrospective consistency
PMD	64.7%
SAD	36.8%
Schizophrenia	69.8%
Bipolar	69.9%
Other	55.1%

Table 7-10 shows the odds ratios, confidence intervals and p values for the proportion of cases who have the same diagnosis at baseline as they did at follow-up (retrospective validity). The table shows strong evidence that SAD cases were less likely to have the same diagnosis at follow-up as they did at baseline compared with schizophrenia cases (OR 0.25, 95% CI 0.10-0.67, p=0.006). There was evidence that SAD cases were less likely to have the same diagnosis at follow-up as they did at baseline compared with bipolar cases (OR 0.25, 95% CI 0.09-0.72, p=0.011). There was evidence that PMD cases were more likely to have the same diagnosis at follow-up as they did at baseline compared with SAD cases (OR 3.14, 95% CI 1.05-9.39, p=0.040).

Table 7-10: Odds ratios, confidence intervals and p values for the proportion of cases who have the same diagnosis at baseline as they did at follow-up (retrospective validity)

	PMD vs. SZ (n276)	PMD vs. BP (n124)	PMD vs. SAD (n70)	SAD vs. SZ (n244)	SAD vs. BP (n92)
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Prospective consistency	0.79 (0.42-1.51)	0.79 (0.37-1.69)	3.14 (1.05-9.39)**	0.25 (0.10-0.67)***	0.25 (0.09-0.72)**

* p<0.1; ** p<0.05; *** p<0.01; CI = 95% confidence interval.

7.4.4. Predictors of diagnostic change

Baseline demographic and clinical variables were examined to see if any of these variables predicted diagnostic change in PMD and SAD (Table 7-11). The analysis of predictors of diagnostic change in SAD was limited by the fact that the numbers of cases included in the analysis were low (n12-18). This resulted in some predictors being incalculable and other variables having very large confidence intervals, therefore it was very difficult to make any conclusions about predictors of change in SAD cases.

The following variables were found to be statistically significantly (at the traditional p<0.05 threshold) associated with diagnostic change in PMD: being younger at first contact (Age: OR 0.91, 95% CI 0.86-0.96, p<0.001; Aged 16-29: OR 6.43, 95% CI 2.10-19.65, p=0.001); being younger at onset (OR 0.90, 95% CI 0.84-0.95, p<0.001) and being single (OR 2.90, 95% CI 1.03-8.17, p=0.044). There are other predictors which have large odds ratios but do not reach statistical significance. This was possibly due to low numbers in the PMD cases in these analyses. These predictors are: being black African (OR 9.0, 95% CI 0.98-83.06) or of other white ethnicity (OR 4.5, 95% CI 0.42-47.76); being born outside the UK (OR 1.93, 95% CI 0.67-5.55, p=0.220); being referred to services via A&E (OR 2.35, 95% CI 0.38-14.47), police or court (OR 2.35, 95% CI 0.38-14.47); and having no family history of psychosis (OR 1.96, 95% CI 0.59-6.52, p=0.272), no family history of general mental illness (OR 2.68, 95% CI 0.61-

11.78, p=0.191), no parental history of psychosis (OR 1.74, 95% CI 0.37-8.18, p=0.481), and no parental history of general mental illness (OR 2.09, 95% CI 0.35-12.51, p=0.421).

Some clinicians have argued that "...early-onset PMD should be considered an initial episode of bipolar disorder until proven otherwise..."[161] Therefore, Table 7-12 presents the predictors of change recalculated without the cases who move from PMD to bipolar disorder. There was no difference in the results with the exception of Black African cases now being 14 times more likely to change from a diagnosis of PMD to another diagnosis at follow-up (OR 14, 95% CI 1.47-133.68, $p<0.05$).

7.4.5. Summary of diagnostic change

In summary, there was evidence that PMD and SAD have lower prospective consistency compared with schizophrenia and bipolar disorder, and that SAD has lower retrospective consistency compared with schizophrenia, bipolar disorder and PMD. The majority of PMD and SAD cases who change diagnosis, change to a diagnosis of schizophrenia as their lifetime diagnosis. Predictors of diagnostic change in PMD are being single, being younger at illness onset and being younger at first contact with services.

Table 7-11: Baseline demographic and clinical predictors of diagnostic change in PMD and SAD cases

	PMD	SAD
Demographics	**OR (CI)**	**OR (CI)**
Age	0.91 (0.86-0.96)*	1.00 (0.91-1.09)
Age dichotomised:		
30-65	-	-
16-29	6.43 (2.10-19.65)*	1.31 (0.19-9.10)
Age at onset	0.90 (0.84-0.95)*	0.99 (0.91-1.08)
Gender:		
Male	-	-
Female	1.06 (0.41-2.76)	0.76 (0.11-5.28)
Ethnicity:		
White British	-	-
Other White	4.5 (0.42-47.76)	$
Black Caribbean	1.5 (0.32-7.01)	0.86 (0.04-16.85)
Black African	9 (0.98-83.06)	$
Asian	1.5 (0.26-8.52)	$
Other	2 (0.39-10.34)	$
Place of birth:		
UK born	-	-
Non UK born	1.93 (0.67-5.55)	$
Living situation:		
Alone	-	-
With others	1.24 (0.45-3.41)	0.28 (0.04-2.08)
Relationship status:		
In a relationship	-	-
Single	2.90 (1.03-8.17)*	1.80 (0.19-16.98)
Clinical variables	**OR (CI)**	**OR (CI)**
Onset of disorder:		
Acute	-	-
Insidious	0.87 (0.31-2.49)	0.21 (0.02-2.52)
Source of Referral:		
GP	-	-
Emergency	0.59 (0.13-2.71)	$
clinic/psychiatrist	2.35 (0.38-14.47)	6.67 (0.49-91.33)
A&E	2.35 (0.38-14.47)	$
Police/Prison/Courts	1.18 (0.21-6.61)	$
Other		
Contact:		
Non-compulsory	-	-
Compulsory	1.56 (0.39-6.13)	0.60 (0.03-11.47)
DUP in days	1.00 (1.00-1.01)	1.00 (1.00-1.00)
Family history of mental illness:		
Yes	-	-
No	1.96 (0.59-6.52)	0.17 (0.01-2.09)
Family history of psychosis:		
Yes	-	-
No	2.68 (0.61-11.78)	0.38 (0.03-4.71)
Parental history of mental illness:		
Yes	-	-
No	1.74 (0.37-8.18)	$
Parental history of psychosis:		
Yes	-	-
No	2.09 (0.35-12.51)	$

*p<0.05; OR=odds ratio; CI=95% confidence interval; $=STATA unable to calculate due to low numbers

Table 7-12: Baseline demographic and clinical predictors of diagnostic change in PMD without cases who moved to bipolar disorder

	PMD
Demographics	**OR (CI)**
Age	0.90 (0.84-0.96)*
Age dichotomised:	
30-65	-
16-29	5.63 (1.75-18.05)*
Age at onset	0.90 (0.85-0.96)*
Gender:	
Male	-
Female	0.75 (0.27-2.09)
Ethnicity:	
White British	-
Other White	7 (0.64-76.71)
Black Caribbean	1.17 (0.18-7.56)
Black African	14 (1.47-133.68)*
Asian	2.33 (0.39-13.85)
Other	3.11 (0.57-16.83)
Place of birth:	
UK born	-
Non UK born	2.50 (0.83-7.51)
Living situation:	
Alone	-
With others	0.83 (0.29-2.37)
Relationship status:	
In a relationship	-
Single	4.53 (1.36-15.07)*
Clinical variables	**OR (CI)**
Onset of disorder:	
Acute	-
Insidious	1.13 (0.37-3.44)
Source of Referral:	
GP	-
Emergency clinic/psychiatrist	0.83 (0.18-3.96)
A&E	3.33 (0.53-21.03)
Police/Prison/Courts	2.50 (0.36-17.17)
Other	1.67 (0.29-9.62)
Contact:	
Non-compulsory	-
Compulsory	1.67 (0.40-6.97)
DUP in days	1.00 (1.00-1.01)
Family history of mental illness:	
Yes	-
No	2.50 (0.65-9.55)
Family history of psychosis:	
Yes	-
No	3.33 (0.61-18.06)
Parental history of mental illness:	
Yes	-
No	2.16 (0.37-12.44)
Parental history of psychosis:	
Yes	-
No	1.65 (0.27-10.02)

*p<0.05; OR = odds ratio; CI = 95% confidence interval.

7.5. Course and outcome by baseline diagnosis

Course of illness and outcome by baseline diagnosis will now be examined.

7.5.1. Course of illness over 10 years by baseline diagnosis

7.5.1.1. Course of illness type by baseline diagnosis

Table 7-13 shows that the bipolar group had the highest proportion of cases with an episodic course of illness and the lowest proportion with a continuous course of illness (number in analyses: 283). The schizophrenia group had the opposite with the lowest proportion of episodic and highest proportion of continuous course of illness. The PMD and SAD groups were between these two. The PMD and SAD group had approximately 50% of cases who had a 'neither episodic nor continuous course' (i.e. episodes lasted over 6 months and remission lasted over 6 months), with around 30-35% having an episodic course and only around 15% having a continuous course.

Table 7-13: Comparison of course of illness variables by baseline diagnosis

	PMD (n51)	SAD (n17)	SZ (n167)	BP (n48)
	N (%)	N (%)	N (%)	N (%)
Course type:				
Episodic	19 (37.3)	5 (29.4)	30 (18.0)	37 (77.1)
Continuous	7 (13.7)	3 (17.7)	56 (33.5)	2 (4.2)
Neither	25 (49.0)	9 (52.9)	81 (48.5)	9 (18.8)

SZ=schizophrenia; BP=bipolar

The hypothesis that PMD and SAD groups have a higher proportion of cases with an episodic course of illness and less with a continuous course of illness compared with schizophrenia cases was tested. There was strong evidence that PMD cases were more likely to have an episodic course of illness (OR 2.71, 95% CI 1.36-5.41, p=0.005) and less likely to have a continuous course of illness (OR 0.32, 95% CI 0.13-0.75, p=0.009) compared with schizophrenia cases (Table 7-14). There was no evidence of any

differences in the course of illness between SAD and schizophrenia cases (episodic: OR 1.90, 95% CI 0.62-5.81, p=0.258; continuous: OR 0.42, 95% CI 0.12-1.54, p=0.192).

There was also strong evidence that PMD cases were less likely to have an episodic course of illness (OR 0.18, 95% CI 0.07-0.43, p<0.001) and more likely to have a 'neither episodic nor continuous' course of illness (OR 4.17, 95% CI 1.68-10.34, p=0.002) compared with bipolar cases. There was strong evidence that SAD cases were less likely to have an episodic course of illness (OR 0.12, CI .04-0.43, p=0.001) and more likely to have a 'neither' course of illness (OR 4.88, 95% CI 1.47-16.13, p=0.009) compared with bipolar cases. There was some evidence that SAD cases were more likely to have a continuous course of illness (OR 4.93, 95% CI 0.75-32.51, p=0.097) compared with bipolar cases. The OR for this finding is high and the fact that the p value is not significant at the traditional p value of 0.05 is possibly due to the lower numbers in this comparison. There was no evidence of any differences in the course of illness between SAD and PMD cases (see Table 7-14).

Table 7-14: OR, CI and p value for comparisons between the groups in the course of illness variable

	PMD vs. SZ (n218)	**PMD vs. BP (n99)**	**PMD vs. SAD (n68)**	**SAD vs. SZ (n184)**	**SAD vs. BP (n65)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Course type: Neither	1.02 (0.55-1.91)	4.17 (1.68-10.34)***	0.85 (0.28-2.57)	1.19 (0.44-3.25)	4.88 (1.47-16.13)***
Course type: Episodic	2.71 (1.36-5.41)***	0.18 (0.07-0.43)***	1.43 (0.43-4.67)	1.90 (0.62-5.81)	0.12 (0.36-0.43)***
Course type: Continuous	0.32 (0.13-0.75)***	3.66 (0.72-18.58)	0.74 (0.17-3.26)	0.42 (0.12-1.54)	4.93 (0.75-32.51)*

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

7.5.1.2. Longest period of remission by baseline diagnosis

Figure 7-1 is a histogram of the longest weeks of remission and shows that the data is not normally distributed. Therefore, medians and interquartile ranges have been used to describe the data. Attempts to transform the data and make it and its residuals normal

were unsuccessful so bootstrap regressions were applied. Table 7-15 shows that the bipolar group had the longest median weeks of remission and schizophrenia had the lowest with PMD and SAD being in between these two (number in analyses: 230).

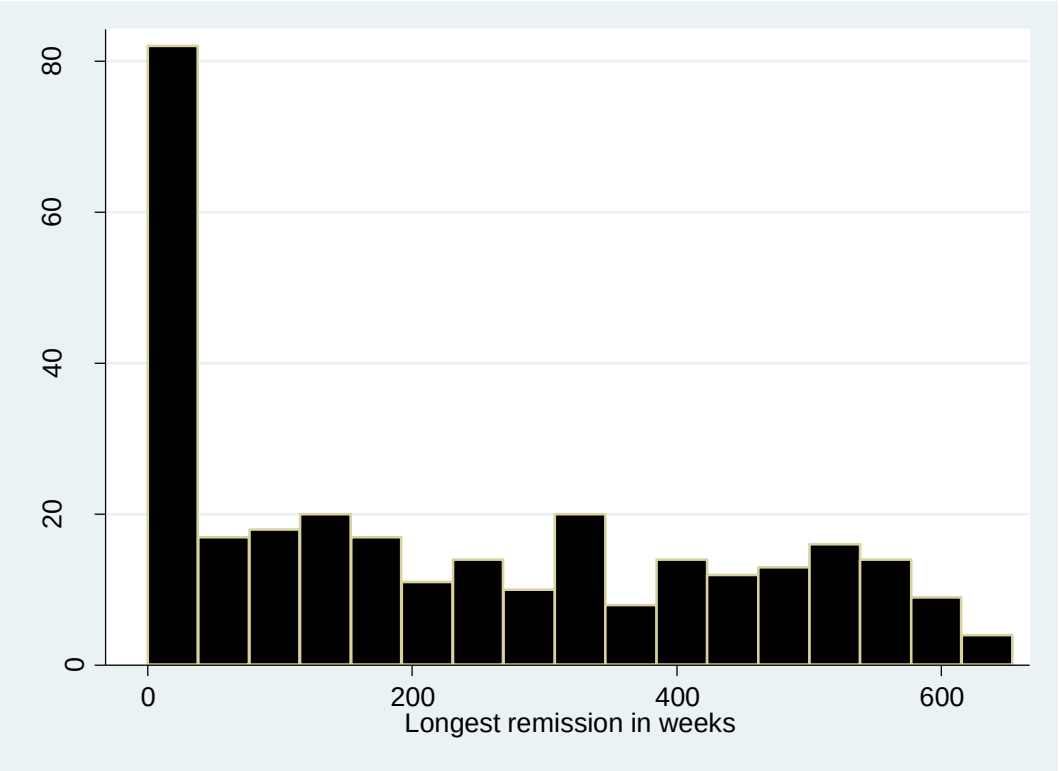


Figure 7-1: Histogram of longest weeks of remission for the core analytic sample with valid data

The hypothesis that PMD and SAD cases would have longer remissions compared with schizophrenia cases was tested. There was strong evidence that PMD cases (beta coefficient 134.17, 95% CI 62.55 to 205.79, p<0.001; Table 7-16), but not SAD cases (beta coefficient 68.94, 95% CI -31.22 to 169.10, p=0.177), had on average a longer period of remission compared with schizophrenia cases. There was evidence that SAD cases had a shorter longest period of remission compared with bipolar cases (beta coefficient -104.30, 95% CI -206.78 to -1.82, p=0.046).

Table 7-15: Comparison of longest weeks of remission by baseline diagnosis

	PMD (n41)	SAD (n13)	SZ (n136)	BP (n40)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Longest weeks of remission	337 (101-468)	210 (120-334)	106 (0-299)	377 (221-469)

IQR = Interquartile range

Table 7-16: Coefficients, CI and p value for comparisons between the groups in the longest weeks of remission variable

	PMD vs. SZ (n177)	PMD vs. BP (n81)	PMD vs. SAD (n54)	SAD vs. SZ (n149)	SAD vs. BP (n53)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Longest weeks of remission	134.17 (62.55 to 205.79)***	-39.08 (-121.39 to 43.24)	65.23 (-46.67 to 177.11)	68.94 (-31.22 to 169.10)	-104.30 (-206.79 to -1.82)**

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

7.5.1.3. Number of episodes by baseline diagnosis

The data on the number of episodes was not normally distributed, therefore, medians and interquartile ranges have been used to describe the data. Number of episodes is count data and as the mean and variance of this outcome indicated that over dispersion was present, a negative binomial regression has been used. Table 7-17 shows that the median number of episodes excluding the first was very similar in all the groups but PMD had the lowest with a median of 0.5 episodes and SAD had the highest with a median of 2 episodes (number in analyses: 177 of the 237 who had a non-continuous course).

The hypothesis that PMD and SAD cases would have more episodes compared with schizophrenia cases was tested. There was strong evidence that the rate at which episodes occurred was 49% less in the PMD group compared with the schizophrenia group (IRR=0.49, 95% CI 0.31-0.76, p=0.001). There was no difference between SAD and schizophrenia cases (IRR=0.80, 95% CI 0.46-1.37, p=0.414). There was also evidence that the rate at which episodes occurred was 55% less in PMD cases compared with bipolar cases (IRR=0.55, 95% CI 0.31-0.99, p=0.046; Table 7-18).

Table 7-17: Comparison of number of episodes by baseline diagnosis

	PMD (n36)	SAD (n13)	SZ (n88)	BP (n40)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Number of episodes	0.5 (0-1)	2 (0-3)	1 (0.5-3)	1 (0-2)

IQR = Interquartile range

Table 7-18: IRR, CI and p value for comparisons between the groups in the number of episodes

	PMD vs. SZ (n124)	PMD vs. BP (n76)	PMD vs. SAD (n49)	SAD vs. SZ (n101)	SAD vs. BP (n53)
	IRR (CI)	IRR (CI)	IRR (CI)	IRR (CI)	IRR (CI)
Number of episodes	0.49 (0.31-0.76)***	0.55 (0.31-0.99)**	0.61 (0.31-1.22)	0.80 (0.46-1.37)	0.90 (0.45-1.80)

*p<0.1; **p<0.05; ***p<0.01; IRR = incidence rate ratio; CI = 95% confidence interval.

7.5.1.4. Months of longest episode by baseline diagnosis

Figure 7-2 is a histogram of the months of longest episode and shows that the data is not normally distributed. Therefore, medians and interquartile ranges have been used to describe the data. Attempts to transform the data and make it and its residuals normal were unsuccessful so bootstrap regressions were applied. Table 7-19 shows that the bipolar group had the lowest median longest episode with three months while the SAD group had the longest with 10 months (number in analyses: 144 of the 237 who had a non-continuous course). The PMD and schizophrenia groups lay in between with a median of seven months for the longest episode.

The hypothesis that PMD and SAD cases would have shorter episodes compared with schizophrenia cases was not supported by the data (Table 7-20). However, there was evidence that compared with bipolar cases, PMD cases (beta coefficient = 15.17, 95% CI 0.19-30.14, p=0.047) and SAD cases (beta coefficient = 10.29, 95% CI 0.67 to 19.92, p=0.036; Table 7-20) had longer time in their longest episode.

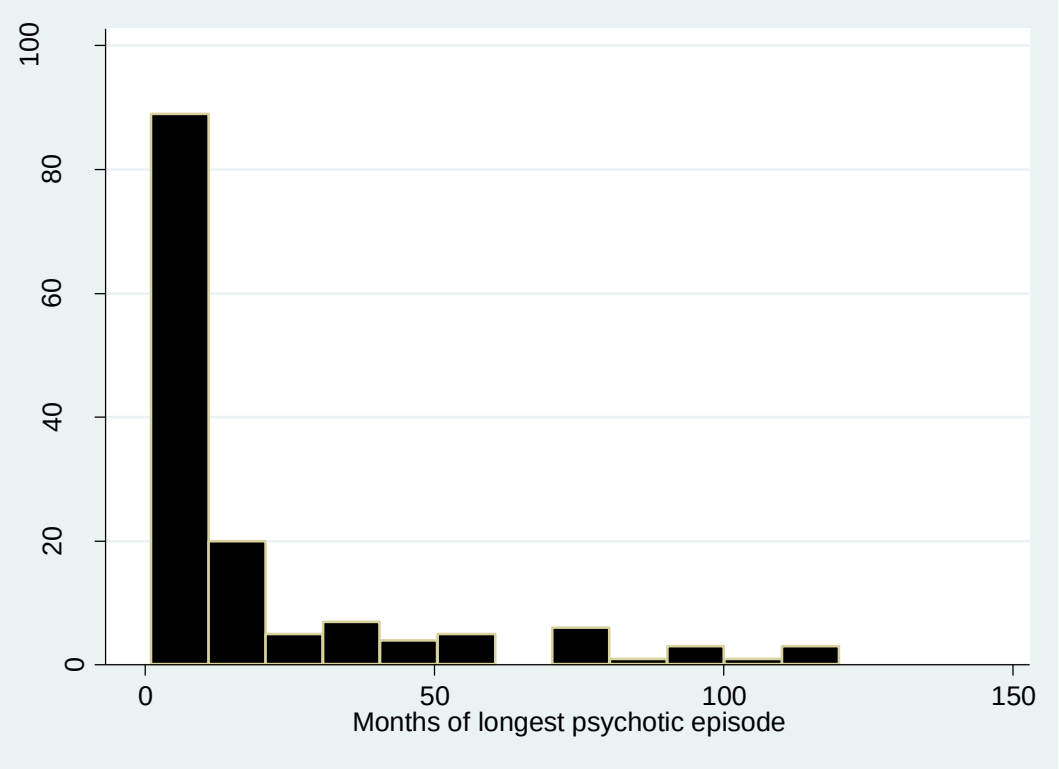


Figure 7-2: Histogram of months of longest episode for the core analytic sample with valid data

Table 7-19: Comparison of longest episode in months by baseline diagnosis

	PMD (n16)	SAD (n8)	SZ (n66)	BP (n24)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Longest episode in months (including first episode)	7 (2-21)	10 (3.5-17)	7 (3-35)	3 (1-4)

IQR = Interquartile range

Table 7-20: Coefficient, CI and p value for comparisons between the groups in the longest episode in months

	PMD vs. SZ (n82)	PMD vs. BP (n40)	PMD vs. SAD (n24)	SAD vs. SZ (n74)	SAD vs. BP (n32)
	Beta coefficient (CI)	Beta coefficient (CI)	Beta coefficient (CI)	Beta coefficient (CI)	Beta coefficient (CI)
Longest episode in months (including first episode)	-5.31 (-21.72 to 11.10)	15.17 (0.19 to 30.14)**	4.88 (-12.64 to 22.39)	-10.19 (-22.81 to 2.44)	10.29 (0.67 to 19.92)**

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

7.5.1.5. Percentage of time psychotic during follow-up by baseline diagnosis

Figure 7-3 is a histogram of the percentage of time psychotic during follow-up and shows that the data is not normally distributed. Therefore, medians and interquartile ranges were used to describe the data. Attempts to transform the data and make it and its residuals normal were unsuccessful so bootstrap regressions have been applied. Table 7-21 shows wide variation in the median percentage of time psychotic over the follow-up from 4.39% in the bipolar group to 48.53% in the schizophrenia group, with the PMD and SAD groups being in between these (number in analyses: 183).

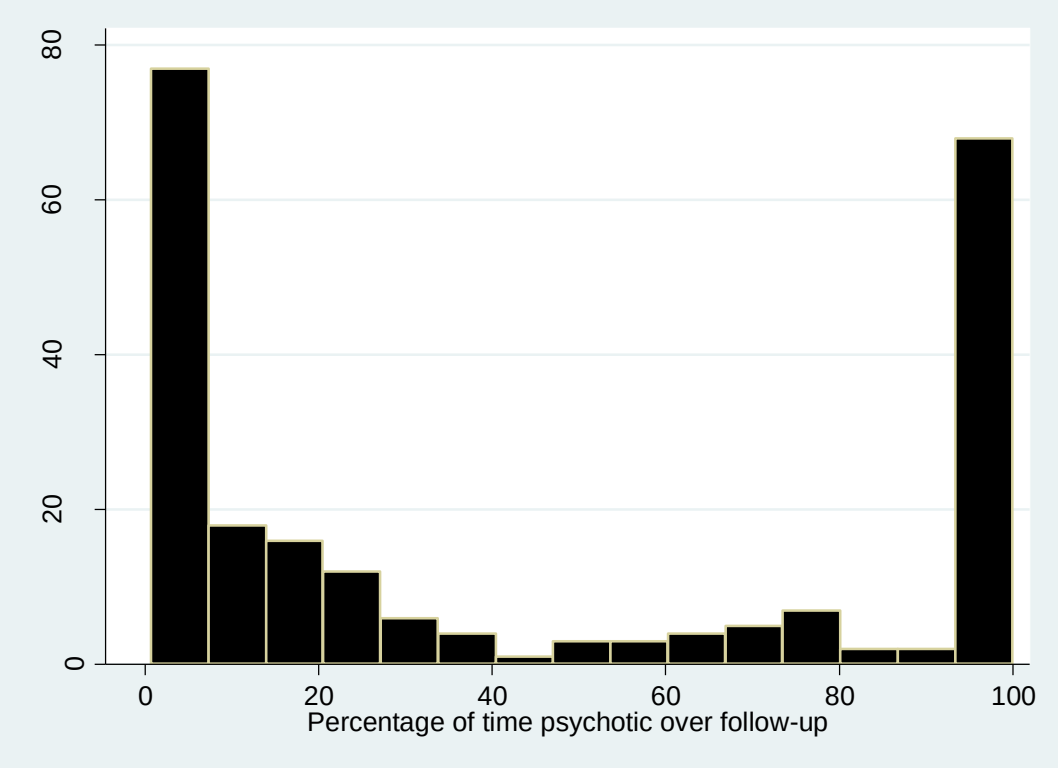


Figure 7-3: Histogram of percentage of time psychotic over follow-up for the core analytic sample with valid data

The hypothesis that PMD and SAD cases would spend a smaller percentage of the follow-up psychotic compared with schizophrenia cases was tested. There was evidence that PMD cases (beta coefficient -17.09, 95% CI -33.35 to -0.82, p=0.039), but not SAD cases (beta coefficient -10.00, 95% CI -34.19 to 20.02, p=0.436), spent less of the

follow-up in a psychotic episode compared with schizophrenia cases. There was also evidence that PMD cases spent more of the follow-up in a psychotic episode compared with bipolar cases (beta coefficient 21.70, 95% CI 5.83 to 37.92, p=0.007; Table 7-22), and that SAD cases spent more time in a psychotic episode compared with bipolar cases (beta coefficient 28.78, 95% CI 3.97 to 53.59, p=0.023).

Table 7-21: Percentage of time psychotic during follow-up by baseline diagnosis

	PMD (n32)	**SAD (n12)**	**SZ (n111)**	**BP (n28)**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Percentage of time psychotic during follow-up	15.78 (4.36-70.83)	20.66 (6.11-89.62)	48.53 (8.40-100)	4.39 (1.69-10.89)

IQR = Interquartile range

Table 7-22: Coefficient, CI and p value for comparisons between the groups in the percentage of time psychotic during follow-up

	PMD vs. SZ (n143)	**PMD vs. BP (n60)**	**PMD vs. SAD (n44)**	**SAD vs. SZ (n123)**	**SAD vs. BP (n40)**
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Percentage of time psychotic during follow-up	-17.09 (-33.35 to -0.82)**	21.70 (5.83 to 37.92)***	-7.08 (-34.19 to 20.02)	-10.00 (-35.17 to 15.16)	28.78 (3.97 to 53.59)**

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

7.5.1.6. Course of illness summary by baseline diagnosis

In summary, of those with a baseline diagnosis of PMD, 37.3% had an episodic course type, 13.7% had a continuous course type and 49% had neither course type. The median longest remission was 337 weeks (101-468 IQR), median number of episodes excluding the first was 0.5 (0-1 IQR), median longest episode was seven months (2-21 IQR) and the median percentage of time in a psychotic episode was 15.78% (4.36-70.83% IQR). For cases with a baseline diagnosis of SAD, 29.4% had an episodic course type, 17.7% had a continuous course type and 52.9% had neither course type. The median longest remission was 210 weeks (120-334 IQR), median number of episodes including the first

was 2 (0-3 IQR), median longest episode was 10 months (3.5-17 IQR) and the median percentage of time in a psychotic episode was 20.66% (6.11-89.62% IQR).

The comparisons revealed evidence that PMD and schizophrenia cases differed from each other on almost every variable on course of outcome. PMD cases: were more episodic and less continuous in course type; had longer remissions; had less episodes; and spent a lower percentage of the follow-up in a psychotic episode, all compared with schizophrenia. There was also some evidence of differences between PMD and bipolar cases. PMD cases: were less episodic in course type and more neither episodic nor continuous; had fewer episodes; had longer longest episodes; and had a higher percentage of time psychotic compared with bipolar cases. There was evidence of differences between SAD and bipolar cases in most of the course of illness variables. SAD cases: were less episodic course type, more continuous course type and more neither continuous nor episodic; had lower longest periods of remission; had longer longest episodes; and had a higher percentage of time psychotic over the follow-up, compared with bipolar cases. Interestingly, no evidence of differences in course type were found between PMD and SAD cases. The results based on the SAD cases must be interpreted with caution due to the low numbers in the SAD group (n8 in some analyses).

7.5.2. Mortality, suicidality and social outcomes at 10 years by baseline diagnosis

7.5.2.1. Mortality and suicidality by diagnosis by baseline diagnosis

7.5.2.1.1. Mortality by baseline diagnosis

Overall, 24 cases (7.7%) died over the follow-up (of the core analytic sample). Table 7-23 shows the percentages of cases who died over follow-up varied from 0% in the

SAD group to 9.9% in the schizophrenia group. The number of deaths in the PMD and bipolar groups fell between these with 5.3% and 5.4% respectively (number in analyses: 312).

Table 7-23: Comparison of numbers and percentages of cases who died by baseline diagnosis

	PMD (n57)	SAD (n18)	SZ (n181)	BP (n56)
	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Dead	3/57 (5.3)	0/18 (0.0)	18/181 (9.9)	3/56 (5.4)

Table 7-24: OR, CI and p value for comparisons between the groups in the proportion of cases who died over follow-up

	PMD vs. SZ (n238)	PMD vs. BP (n113)	PMD vs. SAD (n57)	SAD vs. SZ (n181)	SAD vs. BP (n56)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Death	0.50 (0.14-1.77)	0.98 (0.19-5.08)	$	$	$

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval; $ Unable to calculate odds ratios as no SAD cases died over follow-up.

The hypothesis that PMD and SAD cases would have a higher proportion of cases who died over follow-up compared with schizophrenia and bipolar cases was tested. There was no evidence that any of the groups differed in those who died over the follow-up period (Table 7-24). The comparison of each group to the SAD group was not possible as there were no deaths in the SAD group. However, the chi squared analysis of the whole core analytic sample indicated that there were no differences between the groups in terms of the number of cases who died (chi2=3.70, df3, p=0.443 (fisher's exact)).

7.5.2.1.2. Completed suicide by baseline diagnosis

Data on cause of death was only available for 16 out of the 24 cases who died. Eight of these cases had committed suicide. Due to the very low numbers, there was not enough information to test the hypothesis that PMD and SAD cases would have a higher frequency of completed suicides compared with schizophrenia and bipolar cases.

7.5.2.1.3. Attempted suicide by baseline diagnosis

The data on number of suicide attempts was count data and an examination of the mean and variance indicated over dispersion, therefore, a negative binomial regression has been used. Table 7-25 shows that similar proportions from each group attempted suicide and that the median number of suicide attempts was similar between the groups both when all cases are included and when only those who attempted were included (number in analyses: 270).

Table 7-25: Comparison of the occurrence of suicide attempts and the number of suicide attempts by baseline diagnosis

	PMD (n47)	**SAD (n18)**	**SZ (n159)**	**BP (n46)**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Attempted suicide **Yes** **No**	 11 (23.40) 36 (76.60)	 4 (22.22) 14 (77.78)	 29 (18.35) 129 (81.65)	 9 (19.57) 37 (80.43)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Number of suicide attempts (for all cases not just attempters)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Mean number of suicide attempts (for suicide attempters only)	2 (1-4)	1 (1-1)	1 (1-3)	1 (1-2)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 7-26: OR, CI and p value for comparisons between the groups in the occurrence of suicide attempts and the IRR, CI and p value for comparisons between the groups in the number of suicide attempts

	PMD vs. SZ (n206)	**PMD vs. BP (n93)**	**PMD vs. SAD (n65)**	**SAD vs. SZ (n177)**	**SAD vs. BP (n64)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Attempted suicide	1.37 (0.62-3.01)	1.26 (0.47-3.39)	1.07 (0.29-3.93)	1.28 (0.39-4.18)	1.17 (0.31-4.44)
	IRR (CI)	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**
Suicide attempts (for all cases)	1.88 (0.71-4.93)	1.85 (0.52-6.62)	3.23 (0.63-16.64)	0.57 (0.13-2.53)	0.63 (0.14-2.72)
Suicide attempts (for suicide attempters only)	1.17 (0.71-1.95)	1.46 (0.72-2.97)	2.46 (0.82-7.36)	0.47 (0.17-1.31)	0.60 (0.20-1.81)$

*p<0.1; **p<0.05; ***p<0.01; OR = Odds ratio; IRR = incidence rate ratio; CI = 95% confidence interval.

The hypothesis that PMD and SAD cases would have a higher proportion of cases who attempted suicide over the follow-up, and a higher rate of suicide attempts for those

who do attempt, compared with schizophrenia and bipolar cases was tested. There was no evidence that PMD or SAD differed from bipolar or schizophrenia, or each other, in the occurrence of suicide attempts, or in the number of suicide attempts (Table 7-26).

7.5.2.1.4. Self-harm by baseline diagnosis

Of the 381 included in the core analytic sample, 157 had data on self-harm and therefore form the participants included in this section (the number of self-harm occurrences was missing for one case although self-harm was confirmed therefore the numbers are slightly different in the table (see Table 7-27)). The data on number of events is count data and an examination of the mean and variance indicated over dispersion, therefore, a negative binomial regression has been used.

Table 7-27 shows the occurrence of self-harm by each baseline diagnosis. It shows that the frequency of self-harm varied from 10.9% in the bipolar group to 27.8% in the SAD group with the PMD and schizophrenia group falling between these two at 20.8% and 14.7% respectively. It also shows that the median number of self-harm occurrences was similar between the groups both when all cases are included and when only those who self-harmed were included.

Table 7-27: Comparison of the occurrence of self-harm data by baseline diagnosis

	PMD (n48)	**SAD (n18)**	**SZ (n157)**	**BP (n46)**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Self-harmed				
Yes	10 (20.8)	5 (27.8)	23 (14.7)	5 (10.9)
No	38 (79.2)	13 (72.8)	134 (85.4)	41 (89.1)
	PMD (n48)	**SAD (n18)**	**SZ (n156)**	**BP (n46)**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Mean number of self-harm episodes for all cases not just self-harmers)	0 (0-0)	0 (0-1)	0 (0-0)	0 (0-0)
Mean number of self-harm episodes for self-harmers only)	1 (1-2)	1 (1-1)	1 (1-3)	1 (1-1)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 7-28: OR, IRR, CI and p value for comparisons between the groups in the occurrence of self-harm

	PMD vs. SZ (n205)	**PMD vs. BP (n94)**	**PMD vs. SAD (n66)**	**SAD vs. SZ (n175)**	**SAD vs. BP (n64)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Self-harm	1.53 (0.67-3.50)	2.16 (0.68-6.89)	0.68 (0.20-2.38)	2.24 (0.73-6.88)	3.15 (0.79-12.63)
	PMD vs. SZ (n204)	**PMD vs. BP (n94)**	**PMD vs. SAD (n66)**	**SAD vs. SZ (n174)**	**SAD vs. BP (n64)**
	IRR (CI)	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**
Self-harm (for all cases)	0.94 (0.27-3.22)	3.15 (0.88-11.27)*	1.08 (0.28-4.23)	0.78 (0.13-4.75)	2.85 (0.78-10.40)
Self-harm (for self-harmers only)	0.57 (0.25-1.33)	1.52 (0.60-3.84)	1.36 (0.57-3.26)	0.38 (0.12-1.23)	1.12 (0.38-3.33)

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; IRR = incidence rate ratios; CI = 95% confidence interval.

The hypothesis that PMD and SAD cases would have a higher proportion of cases who self-harmed over the follow-up, and a higher rate of self-harm events for those who do self-harm, compared with schizophrenia and bipolar cases was tested. There was no evidence that PMD and SAD differed from each other or from bipolar or schizophrenia in terms of the occurrence of self-harm (Table 7-28). There was no evidence that the rate at which self-harm events occur differed between PMD and SAD compared with bipolar and schizophrenia, except for one comparison for which there was weak evidence that PMD cases have a higher rate of self-harm events compared with bipolar cases (IRR=3.15, 95% CI 0.88-11.27, p=0.077).

7.5.2.1.5. Mortality and suicidality summary by baseline diagnosis

In summary, of those with a baseline diagnosis of PMD: 5.3% died over follow-up; 23.4% attempted suicide; and 20.8% self-harmed at some point over the follow-up period. For SAD cases: there were no deaths over the follow-up; 22.22% attempted suicide; and 27.8% self-harmed at some point over the follow-up period.

Based on the regression analyses comparing PMD and SAD to each other and to schizophrenia and bipolar, there was no evidence that there were any differences between any of the groups in terms of death, attempted suicide or self-harm, except there was some weak evidence of a difference between PMD cases and bipolar cases in the number of self-harm events.

7.5.2.2. Social outcomes by baseline diagnosis

7.5.2.2.1. Employment status by baseline diagnosis

Table 7-29 shows that the large majority (approximately 75-85%) of SAD and schizophrenia cases were employed for less than 25% of the follow-up (number in analyses: 245). This was lower for PMD and bipolar cases with approximately a half having been employed for less than 25% of the follow-up.

Table 7-29: Comparison of employment outcomes by baseline diagnosis

	PMD (n42)	**SAD (n15)**	**SZ (n150)**	**BP (n38)**
	N (%)	**N (%)**	**N (%)**	**N (%)**
Employment status during fu:				
Employed 75-100%	12 (28.6)	0 (0)	17 (11.3)	9 (23.7)
Employed 50-75%	5 (11.9)	1 (6.7)	10 (6.7)	8 (21.1)
Employed 25-50%	4 (9.5)	1 (6.7)	11 (7.7)	1 (2.6)
Employed 0-25%	21 (50.0)	13 (86.7)	112 (74.7)	20 (52.6)

SZ=schizophrenia; BP=bipolar

Table 7-30: OR, CI and p value for comparisons between the groups of the employment status over the follow-up period

	PMD vs. SZ (n192)	**PMD vs. BP (n80)**	**PMD vs. SAD (n57)**	**SAD vs. SZ (n165)**	**SAD vs. BP (n53)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Employed 0-25%	0.34 (0.17-0.69)***	0.90 (0.37-2.17)	0.15 (0.03-0.77)**	2.21 (0.48-10.22)	5.85 (1.16-29.54)**
Employed 75-100%	3.13 (1.35-7.24)***	1.29 (0.47-3.52)	$	$	$

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval; $ STATA unable to calculate as 0 in the SAD group were employed 75-100% of the time.

The hypothesis that PMD and SAD cases would have a higher proportion of cases who were employed over follow-up compared with schizophrenia cases was tested. There

was strong evidence that compared with schizophrenia cases, PMD cases were less likely to have been employed for 25% or less of the follow-up (OR 0.34, 95% CI 0.17-0.69, p=0.003) and more likely to have been employed for 75% or more of the follow-up (OR 3.13, 95% CI 1.35-7.24, p=0.008; Table 7-30). The finding that SAD cases were over two times more likely than schizophrenia cases to be employed only 0-25% of the follow-up did not reach statistical significance (OR 2.21, 95% CI 0.48-10.22, p=0.312). There was evidence that PMD cases were less likely to have been employed for 25% of less or the follow-up compared with SAD cases (OR 0.15, 95% CI 0.03-0.77, p=0.022), and there was evidence that SAD cases were more likely to have been employed for 25% or less of the follow-up compared with bipolar cases (OR 5.85, 95% CI 16-29.54, p=0.032).

7.5.2.2.2. Relationship status by baseline diagnosis

Table 7-31 shows that both SAD and schizophrenia had the highest percentages (both around 80%) of cases who were mainly single, divorced or separated over the follow-up, with PMD having the lowest at 48.8% (number in analyses: 255).

Table 7-31: Comparison of main relationship status over the follow-up period by baseline diagnosis

	PMD (n41)	**SAD (n15)**	**SZ (n155)**	**BP (n44)**
	N (%)	**N (%)**	**N (%)**	**N (%)**
Main relationship status:				
Single/divorced/separated	20 (48.8)	12 (80.0)	123 (79.4)	24 (54.6)
In a relationship	21 (51.2)	3 (20.0)	32 (20.7)	20 (45.5)

SZ=schizophrenia; BP=bipolar

The hypothesis that PMD and SAD cases would have a higher proportion of cases who were in a relationship over the follow-up compared with schizophrenia cases was tested. There was evidence that PMD cases (OR 4.04, 95% CI 1.95-8.34, p<0.001), but not SAD cases (OR 0.96, 95% CI 0.26-3.61, p=0.953), were more likely to be in a

relationship over the follow-up compared with schizophrenia (Table 7-32). There was also evidence that PMD cases were more likely to be in a relationship over the follow-up compared with SAD cases (OR 4.20, 95% CI 1.03-17.13, p=0.045). There was weaker evidence that SAD was less likely to be in a relationship compared with bipolar cases (OR 0.3, 95% CI 0.07-1.21, p=0.091).

Table 7-32: OR, CI and p value for comparisons between the groups of the main relationship status over the follow-up period

	PMD vs. SZ (n196)	**PMD vs. BP (n85)**	**PMD vs. SAD (n56)**	**SAD vs. SZ (n170)**	**SAD vs. BP (n59)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Relationship status – in a relationship	4.04 (1.95-8.34)***	1.26 (0.54-2.96)	4.20 (1.03-17.13)**	0.96 (0.26-3.61)	0.30 (0.07-1.21)*

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

7.5.2.2.3. Close confidants by baseline diagnosis

Table 7-33 shows that the percentage of cases without a close confidant at follow-up was lowest in bipolar cases with 25% and highest in schizophrenia cases with 46.3% (number in analyses: 137). PMD cases and SAD cases came in between these with 28.6% and 40.0% respectively.

Table 7-33: Comparison of those with close confidants by baseline diagnosis

	PMD (n28)	**SAD (n5)**	**SZ (n80)**	**BP (n24)**
	N (%)	**N (%)**	**N (%)**	**N (%)**
Close confidant:				
Yes	20 (71.4)	3 (60.0)	43 (53.8)	18 (75.0)
No	8 (28.6)	2 (40.0)	37 (46.3)	6 (25.0)

SZ=schizophrenia; BP=bipolar

Table 7-34: OR, CI and p value for comparisons between the groups of the close confidants variable over the follow-up period

	PMD vs. SZ (n108)	**PMD vs. BP (n52)**	**PMD vs. SAD (n33)**	**SAD vs. SZ (n85)**	**SAD vs. BP (n29)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Close confidants	2.15 (0.85-5.45)	0.83 (0.24-2.87)	1.67 (0.23-11.93)	1.29 (0.20-8.15)	0.50 (0.07-3.75)

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

There was no evidence to support the hypothesis that PMD or SAD cases would have a higher proportion of cases with a close confidant over follow-up compared with schizophrenia cases. In fact, there were no differences between any of the groups in those with close confidants (Table 7-34).

7.5.2.2.4. Time in prison by baseline diagnosis

The data on number of months in prison was not normally distributed, therefore, medians and interquartile ranges have been used to describe the data. Attempts to transform the data and make it and its residuals normal were unsuccessful so bootstrap regressions have been applied.

Table 7-35: Comparison of prison contacts by baseline diagnosis

	PMD (n47)	**SAD (n16)**	**SZ (n154)**	**BP (n46)**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Went to prison:				
No	45 (95.7)	15 (93.8)	128 (83.1)	43 (93.5)
Yes	2 (4.3)	1 (6.3)	26 (16.9)	3 (6.5)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Months in prison (for all cases)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Months in prison (for incarcerated cases only)	3.5 (2-5)	60 (60-60)	5 (2-12)	3 (2-4)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 7-35 shows that more schizophrenia cases spent time in prison (16.9%) compared with the other three groups, with the PMD group having the lowest proportion of cases having been to prison (4.3%). The median months spent in prison was similar for all groups when including all cases, but when only including those cases who had been to prison, the SAD group had a much higher median (60 months) compared with the other groups (number in analyses: 263). This is likely due to the low numbers of SAD cases who had been to prison (only one).

Table 7-36: OR, CI and p value for comparisons between the groups for time in prison

	PMD vs. SZ (n201)	PMD vs. BP (n93)	PMD vs. SAD (n63)	SAD vs. SZ (n170)	SAD vs. BP (n62)
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Went to prison	0.22 (0.05-0.96)**	0.64 (0.10-4.00)	0.67 (0.06-7.89)	0.33 (0.04-2.59)	0.96 (0.09-9.90)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Months in prison (for all cases)	-1.45 (-2.48 to -0.43)***	-0.05 (-0.36 to 0.27)	-3.60 (-10.83 to 3.63)	2.15 (-5.04 to 9.33)	3.55 (-3.56 to 10.67)
Months in prison (for incarcerated cases only)	-6.00 (-11.52 to -0.48)**	0.50 (-1.93 to 2.93)	-56.50 (-58.89 to -54.11)***	50.5 (45.53 to 55.47)***	57.00 (55.93 to 58.07)***

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

The hypothesis that PMD and SAD cases would have a lower proportion of cases who had been in prison over the follow-up compared with schizophrenia cases was tested. There was evidence that compared with schizophrenia cases, PMD cases were both less likely to go to prison (OR = 0.22, 95% CI 0.05-0.96, p=0.044) and spent less time in prison over the follow-up period both for those who went to prison (beta coefficient = -6.00, 95% CI -11.52 to -0.48, p=0.033) and for the whole sample (beta coefficient = -1.45, 95% CI -2.48 to -0.43, p=0.005; Table 7-36). There was strong evidence that SAD cases who went to prison over the follow-up spent more time in prison compared with schizophrenia cases (beta coefficient = 50.5, 95% CI 45.53 to 55.47, p<0.001). There was also strong evidence that SAD cases who went to prison over the follow-up spent more time in prison compared with PMD cases (beta coefficient = -56.50, 95% CI -58.89 to -54.11, p<0.001) and bipolar cases (beta coefficient = 57.00, 95% CI 55.93 to 58.07, p<0.001).

7.5.2.2.5. Social outcomes summary by baseline diagnosis

In summary, of those with a baseline diagnosis of PMD, 4.3% had been to prison during some point over the follow-up period, 48.8% were mainly single, divorced or separated

over the follow-up period, and 28.6% had no close confidants. In terms of employment, 28.6% of PMD cases worked for 75-100% of the follow-up period and 50% worked for 0-25% of the follow-up.

Of the cases with a baseline diagnosis of SAD, 6.3% had been to prison during some point over the follow-up period, 80.0% were mainly single, divorced or separated over the follow-up period and 40.0% had no close confidants. In terms of employment, no SAD cases worked for 75-100% of the follow-up period and 86.7% worked for 0-25% of the follow-up.

The comparisons between the groups showed evidence that PMD cases had better outcomes compared with schizophrenia cases on many social outcomes. Compared with schizophrenia cases, PMD cases: were less likely to go to prison; spent less time in prison; were more likely to be in a relationship; and had more time in employment.

There was evidence that PMD cases had better outcomes compared with SAD cases on a number of social outcomes. PMD cases were more likely to be in a relationship, spent more time employed and when examining only those who were incarcerated, PMD cases spent less time in prison. There was also evidence on a few social outcomes that SAD cases had worse outcomes compared with schizophrenia and bipolar cases; when examining only those who were incarcerated, SAD cases spent longer in prison compared with both schizophrenia and bipolar cases; more SAD cases were single/separated/divorced compared with bipolar cases; and SAD cases worked for less time compared with bipolar cases. However, as with the majority of analyses in this chapter, the findings based on SAD cases must be interpreted with caution due to the

low number of cases. For example, when examining months in prison, there was only one case who had been to prison on which to base the analysis.

7.5.3. Service use over 10 years by baseline diagnosis

7.5.3.1. Binary hospitalisation by baseline diagnosis

Table 7-37 shows that the PMD and SAD group have the lowest percentage of cases who were admitted with 84.2% and 88.2% respectively (number in analyses: 308).

Table 7-37: Comparison of hospitalisation data by baseline diagnosis

	PMD (n57)	SAD (n17)	SZ (n180)	BP (n54)
	N (%)	N (%)	N (%)	N (%)
Hospitalisation:				
No admission	9 (15.8)	2 (11.8)	17 (9.4)	2 (3.7)
Admission	48 (84.2)	15 (88.2)	163 (90.6)	52 (96.3)

SZ=schizophrenia; BP=bipolar

There was no evidence to support the hypothesis that PMD and SAD cases would have a lower proportion of cases admitted compared with schizophrenia cases (see Table 7-38). There was some weak evidence that PMD cases were less likely to be hospitalised over the follow-up compared with bipolar cases (OR 0.21, 95% CI 0.04-1.00, p=0.05; Table 7-38).

Table 7-38: OR, CI and p value for comparisons between the groups on hospitalisation

	PMD vs. SZ (n237)	PMD vs. BP (n111)	PMD vs. SAD (n74)	SAD vs. SZ (n197)	SAD vs. BP (n71)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Hospitalisation	0.56 (0.23-1.33)	0.21 (0.04-1.00)*	0.71 (0.14-3.66)	0.78 (0.16-3.71)	0.29 (0.04-2.22)

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

7.5.3.2. Total number of hospitalisations by baseline diagnosis

The data on total number of admissions was not normally distributed so medians and IQRs are presented. The data on total number of hospitalisations is count data and an

examination of the mean and variance indicated over dispersion. Therefore, a negative binomial regression has been used. Table 7-39 shows that the medians and IQRs were all very similar, with PMD cases having a slightly lower median of 1 (number in analyses: 276).

Table 7-39: Comparison of total hospitalisations by baseline diagnosis

	PMD (n50)	**SAD (n17)**	**SZ (n162)**	**BP (n47)**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Total number of hospitalisations	1 (1-3)	2 (1-4)	2 (1-5)	2 (1-4)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 7-40: IRR, CI and p value for comparisons between the groups of the total hospitalisations over the follow-up period

	PMD vs. SZ (n212)	**PMD vs. BP (n97)**	**PMD vs. SAD (n67)**	**SAD vs. SZ (n179)**	**SAD vs. BP (n64)**
	IRR (CI)	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**
Total number of hospitalisations	0.63 (0.46-0.88)***	0.68 (0.47-0.98)**	0.96 (0.57-1.63)	0.66 (0.40-1.08)*	0.72 (0.46-1.12)

*p<0.1; **p<0.05; ***p<0.01; IRR = incidence rate ratio; CI = 95% confidence interval.

The hypothesis that PMD and SAD cases would have less hospitalisations compared with schizophrenia cases was tested. There was strong evidence that the rate at which hospitalisations occur was lower in PMD cases compared with schizophrenia cases (IRR 0.63, 95% CI 0.46-0.88, p=0.006; Table 7-40). There was some weak evidence that the rate at which hospitalisations occur were lower in SAD cases compared with schizophrenia cases (IRR 0.72, 95% CI 0.46-1.12, p=0.095). There was also strong evidence that the rate at which hospitalisations occur was lower in PMD cases compared with bipolar cases (IRR 0.68, 95% CI 0.47-0.98, p=0.041).

7.5.3.3. Total number of days hospitalised by baseline diagnosis

The data on the number of days hospitalised was not normally distributed, thus, medians and IQRs were calculated. Attempts to transform the data and make it and its residuals normal were unsuccessful so bootstrap regressions have been applied. Table 7-41 shows

that the median days were highest for schizophrenia cases at 111.5 days and lowest for PMD cases at 54 days (number in analyses: 235).

Table 7-41: Comparison of days hospitalised by baseline diagnosis

	PMD (n47)	SAD (n15)	SZ (n132)	BP (n41)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Total number of days hospitalised	54 (13-186)	80 (24-191)	115.5 (33-287.7)	73 (27-165)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

The hypothesis that PMD and SAD cases would have less days hospitalised compared with schizophrenia cases was tested. There was strong evidence that PMD cases had less total hospitalisation days over the follow-up compared with schizophrenia cases (beta coefficient -163.62, 95% CI -270.52 to -56.72, p=0.003; Table 7-42). There was no evidence that SAD cases had less total hospitalisation days over the follow-up compared with schizophrenia cases (beta coefficient -50.41, 95% CI -290.07 to 189.26, p=0.686) and there was no evidence of any other differences between the groups.

Table 7-42: Coefficient, CI and p value for comparisons between the groups of the hospitalisation days over the follow-up period

	PMD vs. SZ (n179)	PMD vs. BP (n88)	PMD vs. SAD (n62)	SAD vs. SZ (n147)	SAD vs. BP (n56)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Total number of days hospitalised	-163.62 (-270.52 to -56.72)***	-61.39 (-201.48 to 78.70)	-113.21 (-346.33 to 119.90)	-50.41 (-290.07 to 189.26)	51.83 (-203.83 to 307.48)

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

Figure 7-4 shows the histograms of the number of inpatient days per year by diagnosis. The figure demonstrates that the total number of inpatient days in the first year was similarly high for all diagnoses. Following the first year, the total number of days in each year for PMD was very small in comparison to SAD and schizophrenia. This indicates that the majority of inpatient days are accrued for PMD cases in the first year following first episode of psychosis, but this was not the case for schizophrenia and

SAD cases who have a more even distribution of inpatient days usage. This has important resource implications.

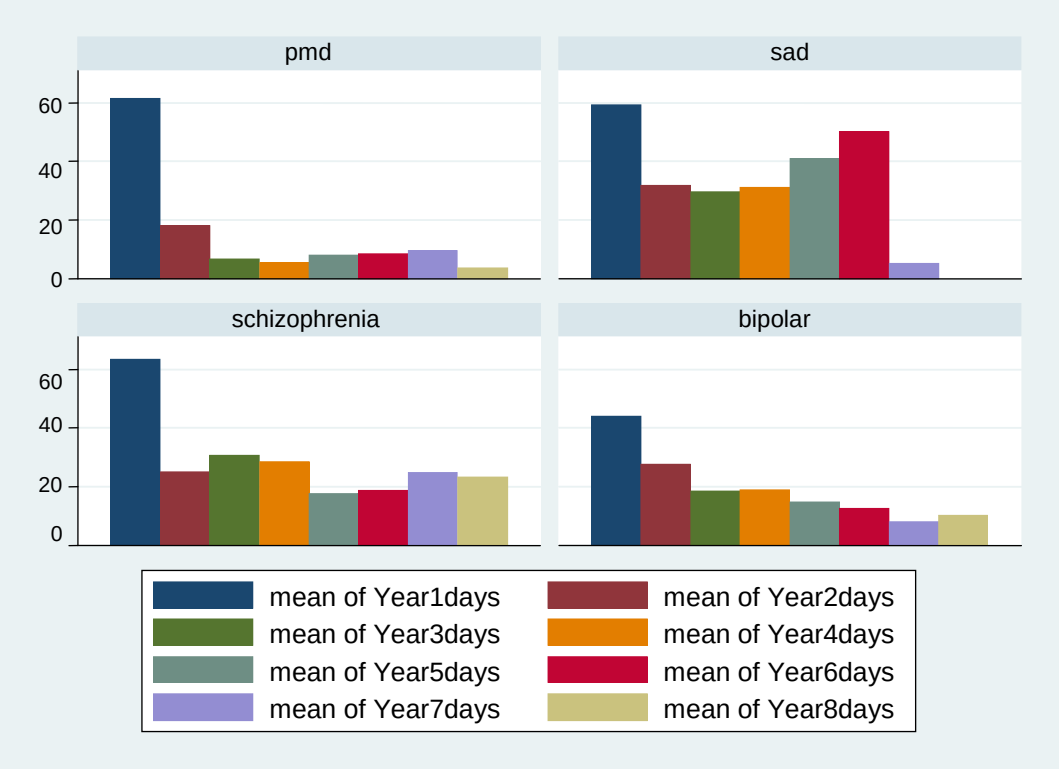


Figure 7-4: Histograms of the number of inpatient days per year by diagnosis

7.5.3.4. Percentage of the follow-up spent as an inpatient by baseline diagnosis

The data on the percentage of follow-up hospitalised was not normally distributed, thus, medians and IQRs were calculated. Attempts to transform the data and make it and its residuals normal were unsuccessful so bootstrap regressions have been applied. Table 7-43 shows that the percentage of the follow-up spent as in inpatient was highest for schizophrenia cases (2.99%) and lowest for PMD cases (1.66%) (number in analyses: 235).

Table 7-43: Comparison of percentage of the follow-up as inpatient data by baseline diagnosis

	PMD (n47)	SAD (n15)	SZ (n132)	BP (n41)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Percentage of follow-up as an inpatient	1.66% (0.46-4.75%)	2.28% (0.63-5.49%)	2.99% (0.85-8.39%)	2.36% (0.72-5.06%)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

The hypothesis that PMD and SAD cases would have a lower a lower percentage of the follow-up spent as an inpatient compared with schizophrenia cases was tested. There was evidence that PMD cases spent less of the follow-up as an inpatient compared with schizophrenia cases (beta coefficient -4.63, 95% CI -8.38 to -0.88, p=0.015; Table 7-44). There was no evidence that SAD cases (beta coefficient -2.12, 95% CI -9.45 to 5.20, p=0.562) spent less of the follow-up as an inpatient compared with schizophrenia cases and there was no evidence of any other differences.

Table 7-44: Coefficient, CI and p value for comparisons between the groups of the percentage as an inpatient over the follow-up period

	PMD vs. SZ (n179)	PMD vs. BP (n88)	PMD vs. SAD (n62)	SAD vs. SZ (n147)	SAD vs. BP (n56)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Percentage of follow-up as an inpatient	-4.63 (-8.38 to -0.88)**	-1.72 (-6.41 to 2.98)	-2.51 (-9.67 to 4.66)	-2.12 (-9.45 to 5.20)	0.79 (-6.85 to 8.44)

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

7.5.3.5. Percentage of admissions which were compulsory by baseline diagnosis

The data on the percentage of admission compulsory was not normally distributed, thus, medians and IQRs were calculated. Attempts to transform the data and make it and its residuals normal were unsuccessful so bootstrap regressions have been applied. Table 7-45 shows that the median percentage for schizophrenia cases was very high at 80% and lowest in the PMD (20%) and SAD (33.3%) cases (number in analyses: 192).

Table 7-45: Comparison of percentage of hospitalisations which were compulsory data by baseline diagnosis

	PMD (n35)	SAD (n11)	SZ (n109)	BP (n37)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Percentage of admissions compulsory	20% (0-100%)	33.3% (0-100%)	80% (25-100%)	66.7% (40-100%)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 7-46: Coefficient, CI and p value for comparisons between the groups of the percentage of hospitalisations which were compulsory over the follow-up period

	PMD vs. SZ (n144)	PMD vs. BP (n72)	PMD vs. SAD (n46)	SAD vs. SZ (n120)	SAD vs. BP (n48)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Percentage of admissions compulsory	-23.29 (-23.29 to -8.89)***	-23.24 (-42.01 to -4.47)**	1.03 (-28.29 to 30.35)	-24.32 (-51.28 to 2.65)*	-24.27 (-52.54 to 4.00)*

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

The hypothesis that PMD and SAD cases would have a lower proportion of cases being compulsorily admitted compared with schizophrenia cases was tested. There was strong evidence that PMD cases had a lower percentage of compulsory admissions compared with schizophrenia cases (beta coefficient -23.29, 95% CI -23.29 to -8.89, p=0.009). There was some weak evidence that SAD cases had a lower percentage of compulsory admissions compared with schizophrenia cases (beta coefficient -24.32, 95% CI -51.28 to 2.65, p=0.077). There was also some evidence that PMD cases had a lower percentage of compulsory admissions compared with bipolar cases (beta coefficient -23.24, 95% CI -42.01 to -4.47, p=0.015; Table 7-46) and some weak evidence that SAD cases had a lower percentage of compulsory admissions compared with bipolar cases (beta coefficient -24.27, 95% CI -52.54 to 4.00, p=0.092).

7.5.3.6. Having ever been admitted compulsorily by baseline diagnosis

Table 7-47 presents data on whether cases were ever compulsorily admitted by baseline diagnoses (number in analyses: 232). PMD (44.4%) and SAD (50.0%) cases had the

lowest percentage of cases who were compulsorily admitted with bipolar cases having the highest percentage (80.5%) being compulsorily admitted.

Table 7-47: Comparison of compulsory hospitalisation data by baseline diagnosis

	PMD (n45)	SAD (n14)	SZ (n132)	BP (n41)
	N (%)	N (%)	N (%)	N (%)
Ever admitted compulsorily:				
No	25 (55.6)	7 (50.0)	40 (30.3)	8 (19.5)
Yes	20 (44.4)	7 (50.0)	92 (69.7)	33 (80.5)

SZ=schizophrenia; BP=bipolar

The hypothesis that PMD and SAD cases would have a lower proportion of cases being compulsorily admitted compared with schizophrenia cases was tested. There was strong evidence that PMD cases were less likely to be compulsorily admitted compared with schizophrenia cases (OR 0.35, 95% CI 0.17-0.70, p=0.003). This was not supported for SAD cases (OR 0.43, 95% CI 0.14-1.32, p=0.142). There was also evidence that PMD cases (OR 0.19, 95% CI 0.07-0.51, p=0.001; Table 7-48) and SAD cases were less likely to be compulsorily admitted compared with bipolar cases (OR 0.24, 95% CI 0.07-0.89, p=0.033).

Table 7-48: OR, CI and p value for comparisons between the groups of compulsory admissions

	PMD vs. SZ (n177)	PMD vs. BP (n86)	PMD vs. SAD (n59)	SAD vs. SZ (n146)	SAD vs. BP (n55)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Compulsory admissions	0.35 (0.17-0.70)***	0.19 (0.07-0.51)***	0.8 (0.24-2.66)	0.43 (0.14-1.32)	0.24 (0.07-0.89)**

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

7.5.3.7. Percentage of hospitalisations involving the police by baseline diagnosis

The data on the percentage of admissions involving the police was not normally distributed, thus, medians and IQRs were calculated. Attempts to transform the data and make it and its residuals normal were unsuccessful so bootstrap regressions have been applied. Table 7-49 shows that the median percentage for each group was zero except the bipolar group which had a median of 27.8% (number in analyses: 207).

Table 7-49: Comparison of police involvement in hospitalisation data by baseline diagnosis

	PMD (n43)	SAD (n11)	SZ (n117)	BP (n36)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Percentage of hospitalisations involving police	0% (0-20%)	0% (0-0%)	0% (0-66.7%)	27.8% (0-70.8%)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 7-50: Coefficient, CI and p value for comparisons between the groups of police involvement in hospitalisations over the follow-up period

	PMD vs. SZ (n160)	PMD vs. BP (n79)	PMD vs. SAD (n54)	SAD vs. SZ (n128)	SAD vs. BP (n47)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Percentage of hospitalisations involving police	-17.23 (-29.35 to -5.10)***	-19.79 (-35.61 to -3.96)**	3.11 (-18.82 to 25.03)	-20.34 (-41.00 to 0.33)*	-22.89 (-46.43 to 0.64)*

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

The hypothesis that PMD and SAD cases would have a lower percentage of hospitalisations involving the police compared with schizophrenia cases was tested. There was evidence that the PMD group had a lower percentage of hospitalisations involving the police that schizophrenia cases (beta coefficient -17.23, -29.35 to -5.10, p=0.005). There was some weak evidence that the SAD group had a lower percentage of hospitalisations involving the police than schizophrenia cases (beta coefficient -20.34, 95% CI -41.00 to 0.33, p=0.054). There was evidence that PMD cases had a lower percentage of hospitalisations involving the police compared with bipolar cases (beta coefficient -19.79, -35.61 to -3.96, p=0.014; Table 7-50) and some weak evidence for the same in SAD cases (beta coefficient -22.89, 95% CI -46.43 to 0.64, p=0.057).

7.5.3.8. Summary of service use by baseline diagnosis

In summary, of those with a baseline diagnosis of PMD, 84.2% had an admission over the follow-up, the median number of admissions was 1 (1-3 IQR), the median number of days hospitalised was 54 (13-186 IQR), the median percentage of the follow-up spent

as an inpatient was 1.66% (0.46-4.75% IQR), the median percentage of admissions which were compulsory was 20.0% (0-100% IQR), 55.6% were never admitted compulsorily and the median percentage of hospitalisations involving the police was 0% (0-20% IQR).

Of those with a baseline diagnosis of SAD, 88.2% had an admission over the follow-up, the median number of admissions was 2 (1-4 IQR), the median number of days hospitalised was 80 (24-191 IQR), the median percentage of days spent as an inpatient was 2.28% (0.63-5.49% IQR), the median percentage of admissions which were compulsory was 33.3% (0-100% IQR), 50.0% were never admitted compulsorily and the median percentage of hospitalisations involving the police was 0% (0-0% IQR).

The comparisons between the groups showed that there was evidence that PMD cases had better outcomes on most of the service use outcomes compared with schizophrenia cases and bipolar cases. Compared with schizophrenia cases, PMD cases had: less total hospitalisations; less total days hospitalised; a lower percentage of the follow-up as an inpatient; less compulsory admissions; and had fewer admissions involving the police. Compared with bipolar cases, PMD cases: were less likely to be admitted; had less total hospitalisations; had less compulsory admissions; and had fewer admissions involving the police.

There was only some weak evidence of differences between SAD, schizophrenia and bipolar cases on a few service use outcomes. There was no evidence of any differences between PMD and SAD cases on service use outcomes.

7.6. Course and outcome by lifetime diagnosis

7.6.1. Course of illness over 10 years by lifetime diagnosis

7.6.1.1. Basic comparison of course type by lifetime diagnosis

There were some small differences in the findings between the analyses based on baseline and lifetime diagnoses. Table 7-51 shows that PMD and bipolar cases were mostly episodic or 'neither episodic nor continuous' in course type (number in analyses: 298). SAD and schizophrenia cases had mostly neither episodic nor continuous course type.

Table 7-51: Comparison of course of illness variables by lifetime diagnosis

	PMD (n39)	**SAD (n15)**	**SZ (n184)**	**BP (n60)**
	N (%)	**N (%)**	**N (%)**	**N (%)**
Course type:				
Episodic	21 (53.9)	4 (26.7)	27(14.7)	44 (73.3)
Continuous	2 (5.1)	3 (20.0)	68(37.0)	0 (0)
Neither	16 (41.0)	8 (53.3)	89 (48.4)	16 (26.7)

SZ=schizophrenia; BP=bipolar

The hypothesis that PMD and SAD cases would have a higher proportion of cases with an episodic course of illness and less with a continuous course of illness compared with schizophrenia cases was tested. There was evidence that PMD cases were more likely to be episodic in course type (OR 6.78, 95% CI 3.20-14.37, p<0.001) and less likely to be continuous (OR 0.09, 95% CI 0.02-0.39, p=0.001) in comparison to schizophrenia cases (Table 7-52). There was no evidence of any differences in course type between SAD and schizophrenia cases (episodic: OR 0.43, 95% CI 0.12-1.56, p=0.199; continuous: OR 1.22, 95% CI 0.42-3.50, p=0.712). There was some weak evidence that PMD cases were more likely to have an episodic course type compared with SAD cases (OR 3.21, 95% CI 0.87-11.84, p=0.08). There was evidence that SAD cases were less likely to have an episodic course type compared with bipolar cases (OR 0.13, 95% CI 0.04-0.48,

p=0.002) and there was weak evidence that they were more likely to have a course type of neither episodic nor continuous (OR 3.14, 95% CI 0.98-10.07, p=0.054).

Table 7-52: OR, CI and p value for comparisons between the groups in the course of illness variable

	PMD vs. SZ (n223)	PMD vs. BP (n99)	PMD vs. SAD (n54)	SAD vs. SZ (n199)	SAD vs. BP (n75)
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Course type: Neither	0.74 (0.37-1.50)	1.91 (0.81-4.51)	0.61 (0.18-2.02)	1.22 (0.42-3.50)	3.14 (0.98-10.07)*
Course type: Episodic	6.78 (3.20-14.37)***	0.42 (0.18-0.99)**	3.21 (0.87-11.84)*	2.11 (0.63-7.13)	0.13 (0.04-0.48)**
Course type: Continuous	0.09 (0.02-0.39)***	$	0.22 (0.03-1.45)	0.43 (0.12-1.56)	$

*p<0.1; **p<0.05; ***p<0.01; OR = Odds ratio; CI = 95% confidence interval; $ STATA unable to calculate as one group with zero cases.

The findings which differ from the baseline analyses were that there was no longer evidence of a difference between PMD and bipolar cases in the occurrence of neither episodic nor continuous life course. There was also evidence of a difference between PMD and SAD in the occurrence of episodic course types that did not exist based on the baseline diagnoses.

7.6.1.2. Longest period of remission by lifetime diagnosis

There was a difference in the findings between the analyses based on baseline and lifetime diagnoses. Table 7-53 shows that PMD cases had the greatest median longest period of remission at 372 weeks with schizophrenia cases having the lowest at 83.5 weeks (number in analyses: 249). SAD and bipolar cases had a median between these at 178 weeks and 360 weeks respectively.

Table 7-53: Comparison of longest weeks of remission by lifetime diagnosis

	PMD (n31)	SAD (n12)	SZ (n154)	BP (n52)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Longest period of remission in weeks	372 (255-533)	178 (39-293)	83.5 (0-230)	360 (213.5-475.5)

IQR = Interquartile range

The hypothesis that PMD and SAD would have longer remissions compared with schizophrenia cases was tested. There was strong evidence that PMD cases had higher longest weeks of remission compared with schizophrenia cases (beta coefficient 228.59, 95% CI 157.85-299.33, p<0.001). There was no evidence for such a difference between SAD and schizophrenia cases (beta coefficient 46.76, 95% CI -46.95 to 146.46, p=0.313). There was also strong evidence that PMD cases had higher longest weeks of remission compared with SAD cases (beta coefficient 178.83, 95% CI 62.04 to 286.31, p=0.003; Table 7-54) and there was strong evidence that SAD cases had lower longest weeks of remission compared with bipolar cases (beta coefficient -154.12, 95% CI -258.55 to -49.68, p=0.004).

Table 7-54: Coefficients, CI and p value for comparisons between the groups in the longest weeks of remission variable

	PMD vs. SZ (n185)	**PMD vs. BP (n83)**	**PMD vs. SAD (n43)**	**SAD vs. SZ (n166)**	**SAD vs. BP (n64)**
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Longest weeks of remission	228.59 (157.85-299.33)***	24.72 (-54.90 to 104.33)	178.83 (62.04 to 295.63)***	49.76 (-46.95 to 146.46)	-154.12 (-258.55 to -49.68)***

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

The finding that PMD cases had higher longest weeks of remission compared with SAD cases was not evident in the analyses based on baseline diagnoses; however, the other two significant findings were identified by the baseline diagnosis analyses.

7.6.1.3. Number of episodes by lifetime diagnosis

There was a difference in the findings between the analyses based on baseline and lifetime diagnoses. Of the 368 included in the core analytic sample, 248 cases had a non-continuous course of illness. Of those, 185 had data on number of episodes and therefore form the participants included in this section. Table 7-55 shows that the median number of episodes excluding the first was lowest in the PMD group at zero

episodes and highest in the SAD group at three episodes (number in analyses: 185 (248 had a non-continuous course).

Table 7-55: Comparison of number of episodes by lifetime diagnosis

	PMD (n31)	SAD (n11)	SZ (n90)	BP (n53)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Number of episodes	0 (0-1)	3 (1-3)	2 (1-3)	1 (0-2)

IQR = Interquartile range

The hypothesis that PMD and SAD cases would have more episodes compared with schizophrenia cases was tested. There was strong evidence that the rate at which episodes occurred were 40% less in the PMD group compared with the schizophrenia group (IRR 0.40, 95% CI 0.25 – 0.65, p<0.001) but not in SAD compared with schizophrenia cases (IRR 1.01, 95% CI 0.60-1.70, p=0.976). There was strong evidence that the rate at which episodes occurred were 53% less in PMD cases compared with bipolar (IRR 0.53, 95% CI 0.29-0.96, p=0.037; Table 7-56). There was also evidence that the rate at which episodes occurred were 40% less in the PMD group compared with the SAD group (IRR 0.40, 95% CI 0.19-0.85, p=0.017).

The finding that PMD cases experienced episodes at a rate of 40% less than SAD cases was not evidenced in the analyses based on the baseline diagnoses; however, the other two significant findings were identified by the baseline diagnosis analyses.

Table 7-56: IRR, CI and p value for comparisons between the groups in the average number of episodes

	PMD vs. SZ (n121)	PMD vs. BP (n84)	PMD vs. SAD (n42)	SAD vs. SZ (n101)	SAD vs. BP (n64)
	IRR (CI)	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**
Number of episodes	0.40 (0.25 – 0.65)***	0.53 (0.29-0.96)**	0.40 (0.19-0.85)**	1.01 (0.60-1.70)	1.33 (0.71-2.46)

*p<0.1; **p<0.05; ***p<0.01; IRR = incidence rate ratio; CI = 95% confidence interval.

7.6.1.4. Months of longest episode by lifetime diagnosis

There was a difference in the findings between the analyses based on baseline and lifetime diagnoses. Table 7-57 shows that the bipolar group had the lowest median length of longest episode at 2 months and schizophrenia cases had the highest at 11 months. PMD and SAD cases came between these: both had a median of 5 months (number in analyses: 124 (248 had a non-continuous course).

Table 7-57: Comparison of average length of longest episode by lifetime diagnosis

	PMD (n13)	**SAD (n9)**	**SZ (n69)**	**BP (n33)**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Length of longest episode in months (including first episode)	5 (1-12)	5 (2-26)	11 (5-43)	2 (1-4)

IQR = Interquartile range

The hypothesis that PMD and SAD would have shorter episodes compared with schizophrenia cases was tested. There was strong evidence that PMD cases had lower longest episodes compared with schizophrenia cases (beta coefficient -17.84, 95% CI -28.33 to -7.36, p=0.001; Table 7-58) but there was no evidence for this difference between SAD and schizophrenia cases (beta coefficient -7.64, 95% CI -25.90 to 10.63, p=0.412).

Table 7-58: Coefficients, CI and p value for comparisons between the groups in the longest episode in months

	PMD vs. SZ (n82)	**PMD vs. BP (n46)**	**PMD vs. SAD (n22)**	**SAD vs. SZ (n78)**	**SAD vs. BP (n42)**
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Longest episode in months (including first episode)	-17.84 (-28.33 to -7.36)***	3.16 (-5.06 to 11.38)	-10.21 (-27.03 to 6.62	-7.64 (-25.90 to 10.63)	13.36 (-4.20 to 30.93)

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

The finding from these lifetime diagnosis analyses that PMD cases had lower longest episodes compared with schizophrenia cases was not found in the baseline diagnosis

analyses. The baseline diagnosis analyses reported that PMD cases and SAD cases had longer longest episodes of illness compared with bipolar cases: this was not supported by the lifetime diagnosis analyses.

7.6.1.5. Percentage of time psychotic during follow-up by lifetime diagnosis

There were differences in the findings between the analyses based on baseline and lifetime diagnoses. Table 7-59 shows that the percentage of time psychotic was very low for PMD and bipolar cases; 5.1% and 3.8% respectively. Comparatively, the percentage of time psychotic was very high for SAD and schizophrenia cases; 52.9% and 76.7% respectively (number in analyses: 189).

The hypothesis that PMD and SAD would spend a smaller percentage of the follow-up psychotic compared with schizophrenia cases was tested. There was strong evidence that PMD cases spent a lower percentage of time psychotic over follow-up compared with schizophrenia cases (beta coefficient -41.53, 95% CI -53.77 to -29.28, p<0.001) but there was no evidence for this in SAD compared with schizophrenia cases (beta coefficient -6.64, 95% CI -38.06 to 24.78, p=0.675). There was strong evidence that PMD cases spent a lower percentage of time psychotic over follow-up compared with SAD cases (beta coefficient -34.89, 95% CI -67.19 to -2.60, p=0.034; Table 7-60). There was strong evidence that SAD cases spent a higher percentage of time psychotic over follow-up compared with bipolar cases (beta coefficient 43.14, 95% CI 10.99 to 75.29, p=0.009).

Table 7-59: Comparison of percentage of time in psychotic episode over follow-up by lifetime diagnosis

	PMD (n25)	**SAD (n8)**	**SZ (n124)**	**BP (n32)**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Percentage of time in psychotic episode in follow-up	5.1% (2.9-21.4)	52.9% (6.6-100)	76.7% (13.1-100)	3.8% (1.7-7.8)

IQR = Interquartile range

Table 7-60: Coefficients, CI and p value for comparisons between the groups in the percentage of time psychotic during follow-up

	PMD vs. SZ (n149)	PMD vs. BP (n57)	PMD vs. SAD (n33)	SAD vs. SZ (n132)	SAD vs. BP (n40)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Percentage of time psychotic during follow-up	-41.53 (-53.77 to -29.28)***	8.25 (-3.21 to 19.71)	-34.89 (-67.19 to -2.60)**	-6.64 (-38.06 to 24.78)	43.14 (10.99 to 75.29)***

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

The findings that schizophrenia cases and SAD cases spent a higher percentage of time psychotic over follow-up compared with PMD cases and bipolar cases consecutively was also found in the baseline diagnosis analyses. However, the finding from the lifetime diagnosis analyses that SAD cases had a higher percentage of time psychotic compared with PMD cases was not found in the baseline diagnosis analyses. The finding from the baseline diagnosis analyses that PMD cases spend more time psychotic compared with bipolar cases was not supported by the lifetime diagnosis analyses.

7.6.1.6. Course of illness summary by lifetime diagnosis

The course of illness analyses based on lifetime diagnoses found some noteworthy differences from the baseline diagnosis analyses. Firstly, there was evidence of some differences between PMD and SAD cases. There was evidence that compared with SAD cases, PMD cases: were more likely to have an episodic course type (albeit weak evidence); had higher longest weeks of remission; had fewer episodes; and spent less time psychotic over the follow-up.

Other findings which differed were: there was no longer evidence of a difference between PMD and bipolar cases in the occurrence of the 'neither episodic or continuous' course of illness; there was new evidence that PMD cases had lower longest episodes compared with schizophrenia cases; there was no longer evidence that PMD

cases and SAD cases had longer longest episodes of illness compared with bipolar cases; and there was no longer evidence that PMD cases spent more time psychotic compared with bipolar cases.

7.6.2. Mortality, suicidality and social outcomes at 10 years by lifetime diagnosis

7.6.2.1. Mortality and suicidality by lifetime diagnosis

The analyses on death based on lifetime diagnoses had the same findings as those based on the baseline diagnoses (see Appendix A; any results based on lifetime diagnoses that show the same findings as the baseline analyses will be placed in the appendices). However, there were some differences in the findings on attempted suicide and self-harm.

7.6.2.1.1. Attempted suicide by lifetime diagnosis

Table 7-61 shows the highest percentage of suicide attempters were in the PMD group (37.1%), followed by the SAD group (29.4%). The number of suicide attempts for those who did attempt suicide was highest in the PMD (median 2) and SAD (median 3) groups (number in analyses: 248).

The hypothesis that PMD and SAD cases would have a higher proportion of cases who attempted suicide over the follow-up, and a higher rate of suicide attempts for those who do attempt, compared with schizophrenia and bipolar cases was tested. There was strong evidence that cases with a lifetime diagnosis of PMD were 2.86 times more likely to attempt suicide compared with schizophrenia cases (OR 2.86, 95% CI 1.30-6.30, p=0.009; Table 7-62). There was some weak evidence that PMD cases were 2.22 times more likely to attempt suicide compared with bipolar cases (OR 2.22, 95% CI

0.87-5.65, p=0.096). There was no evidence that SAD cases were more likely to attempt suicide compared with schizophrenia (OR 2.01, 95% CI 0.66-6.14, p=0.218) and bipolar cases (OR 1.56, 95% CI 0.46-5.30, p=0.474). In terms of number of attempts for the whole sample, there was evidence that PMD cases had a greater rate of suicide attempts compared with schizophrenia cases (IRR 3.55, 95% CI 1.38-9.12, p=0.008) and bipolar cases (IRR 3.17, 95% CI 1.14-8.83, p=0.028). There was some weak evidence that SAD cases had a greater rate of suicide attempts compared with schizophrenia cases (IRR 2.93, 95% CI 0.85-10.16, p=0.090). When only those cases who attempted suicide were included, there was evidence that SAD cases had a greater rate of suicide attempts compared with schizophrenia cases (IRR 1.78, 95% CI 1.03-3.06, p=0.038) and bipolar cases (IRR 2.13, 95% CI 1.09-4.16, p=0.028). When only those cases who attempted suicide were included, there was no evidence that PMD cases had a greater rate of suicide attempts compared with schizophrenia cases (IRR 1.28, 95% CI 0.81-2.04, p=0.293) and bipolar cases (IRR 1.54, 95% CI 0.83-2.83, p=0.169).

Table 7-61: Comparison of suicide attempts by lifetime diagnosis

	PMD (n35)	**SAD (n17)**	**SZ (n175)**	**BP (n57)**
	n/N (%)	**n/N (%)**	**n/N (%)**	**n/N (%)**
Attempted suicide: Yes No	 13 (37.1) 22 (62.9)	 5 (29.4) 12 (70.6)	 30 (17.1) 145 (82.9)	 12 (21.1) 45 (79.0)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Number of suicide attempts (for all cases not just attempters)	0 (0-1)	0 (0-1)	0 (0-0)	0 (0-0)
Number of suicide attempts (for suicide attempters only)	2 (1-3)	3 (2-4)	1 (1-2)	1 (1-1.5)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

These findings are very different from the findings based on the baseline diagnoses which found no differences in the occurrence of self-harm between the groups, or in the number of attempts.

Table 7-62: OR, CI and p value for comparisons between the groups in the occurrence of suicide attempts and the IRR, CI and p value for comparisons between the groups in the number of suicide attempts

	PMD vs. SZ (n210)	PMD vs. BP (n92)	PMD vs. SAD (n52)	SAD vs. SZ (n192)	SAD vs. BP (n74)
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Attempted suicide	2.86 (1.30-6.30)***	2.22 (0.87-5.65)*	1.42 (0.41-4.94)	2.01 (0.66-6.14)	1.56 (0.46-5.30)
	IRR (CI)	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**
Suicide attempts (for all cases)	3.55 (1.38-9.12)***	3.17 (1.14-8.83)**	1.18 (0.31-4.42)	2.93 (0.85-10.16)*	2.72 (0.76-9.69)
Suicide attempts (for suicide attempters only)	1.28 (0.81-2.04)	1.54 (0.83-2.83)	0.74 (0.38-1.47)	1.78 (1.03-3.06)**	2.13 (1.09-4.16)**

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; IRR = incidence rate ratio; CI = 95% confidence interval.

7.6.2.1.2. Self-harm by lifetime diagnosis

Table 7-63 that SAD cases had the highest percentage of self-harmers with 35.3%, followed by PMD cases with 27%. It also shows that PMD cases had the highest median number of self-harm occurrences for those who did self-harm (number in analyses: 283).

The hypothesis that PMD and SAD cases would have a higher proportion of cases who self-harmed over the follow-up, and a higher rate of self-harm events for those who do self-harm, compared with schizophrenia and bipolar cases was tested. There was some evidence that the SAD cases were 3.41 times more likely to self-harm compared with the schizophrenia group (OR 3.41, 95% CI 1.15-10.08, p=0.027; Table 7-64). There was some weak evidence that the PMD group was more likely to self-harm compared with the schizophrenia cases (OR 2.31, 95% CI 1.00-5.38, p=0.051). There was also some weak evidence that the SAD group were more likely to self-harm compared with the bipolar group (OR 3.20, 95% CI 0.92-11.14, p=0.067) but not for PMD cases (OR 2.18, 95% CI 0.77-6.18, p=0.144). In terms of number of self-harm events for the whole sample, there was evidence that PMD (IRR 6.16, 95% CI 1.80-21.03, p=0.004) and

SAD (IRR 5.87, 95% CI 0.77-6.18, p=0.004) cases had a greater rate of self-harm events compared with bipolar cases but not compared to schizophrenia cases. When only those who self-harmed were included, there was evidence that PMD had a greater rate of self-harm events compared with bipolar cases (IRR 3.47, 95% CI 1.52-7.93, p=0.003) and weak evidence that SAD cases had a greater rate of self-harm events compared with bipolar cases (IRR 2.51, 95% CI 0.98-6.43, p=0.054), but again there were no differences compared to the schizophrenia group (PMD: IRR 1.43, 95% CI 0.63-3.24, p=0.394; SAD: IRR 0.97, 95% CI 0.36-2.59, p=0.948).

Table 7-63: Comparison of self-harm data by lifetime diagnosis

	PMD (n37)	**SAD (n17)**	**SZ (n174)**	**BP (n55)**
	n/N (%)	**n/N (%)**	**n/N (%)**	**n/N (%)**
Self-harmed Yes No	 10 (27.0) 27 (73.0)	 6 (35.3) 11 (64.7)	 24 (13.8) 150 (86.2)	 8 (14.6) 47 (85.5)
	PMD (n36)	**SAD (n17)**	**SZ (n174)**	**BP (n55)**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Number of self-harm episodes for all cases not just self-harmers)	0 (0-0.5)	0 (0-1)	0 (0-0)	0 (0-0)
Number of self-harm episodes for self-harmers only)	3 (1-5)	1.5 (1-3)	1 (1-2)	1 (1-1)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 7-64: OR, CI and p value for comparisons between the groups in the occurrence of self-harm and the IRR, CI and p value for comparisons between the groups in the number of self-harm events

	PMD vs. SZ (n211)	**PMD vs. BP (n92)**	**PMD vs. SAD (n54)**	**SAD vs. SZ (n191)**	**SAD vs. BP (n72)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Self-harm	2.31 (1.00-5.38)*	2.18 (0.77-6.18)	0.68 (0.20-2.330	3.41 (1.15-10.08)**	3.20 (0.92-11.14)*
	PMD vs. SZ (n210)	**PMD vs. BP (n91)**	**PMD vs. SAD (n53)**	**SAD vs. SZ (n191)**	**SAD vs. BP (n72)**
	IRR (CI)	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**	**IRR (CI)**
Self-harm (for all cases)	2.72 (0.76-9.66)	6.16 (1.80-21.03)***	1.06 (0.23-4.84)	2.47 (0.47-13.08)	5.87 (1.77-19.51)***
Self-harm (for self-harmers only)	1.43 (0.63-3.24)	3.47 (1.52-7.93)***	1.42 (0.59-3.43)	0.97 (0.36-2.59)	2.51 (0.98-6.43)*

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; IRR = incidence rate ratio; CI = 95% confidence interval.

Like the lifetime diagnosis analyses on suicide attempts, the results on self-harm are very different from those based on the baseline diagnosis analyses which found weak evidence of only one difference between PMD and bipolar cases.

7.6.2.1.3. Mortality and suicidality summary by lifetime diagnosis

The baseline diagnosis analyses found no differences between any of the groups in death, suicide attempts and self-harm. In contrast, the analyses based on the lifetime diagnoses found evidence of many differences between the groups in suicide attempts and self-harm. There was evidence to varying degrees that PMD cases had worse outcomes compared with schizophrenia and bipolar cases in attempted suicide and self-harm outcomes. There was also evidence to varying degrees that SAD cases had worse outcomes compared with schizophrenia and bipolar cases in attempted suicide and self-harm outcomes. There was no evidence of any differences between PMD and SAD cases in attempted suicide and self-harm outcomes.

7.6.2.2. Social outcomes by diagnosis by lifetime diagnosis

7.6.2.2.1. Employment status by lifetime diagnosis

There were no differences in the findings on employment status in the baseline and lifetime diagnosis analyses (Appendix A).

7.6.2.2.2. Relationship status by lifetime diagnosis

Table 7-65 shows that PMD and bipolar cases had the highest percentage of cases who were in a relationship (approximately 52% for both). This was followed by SAD cases of whom 43.8% were in a relationship and finally schizophrenia cases, only 19.2% of whom were in a relationship (number in analyses: 273).

Table 7-65: Comparison of relationship status by lifetime diagnosis

	PMD (n33)	SAD (n16)	SZ (n172)	BP (n52)
	n (%)	n (%)	n (%)	n (%)
Main relationship status – dichotomised:				
Single/divorced/separated	16 (48.5)	9 (56.3)	139 (80.8)	25 (48.1)
In a relationship	17 (51.5)	7 (43.8)	33 (19.2)	27 (51.9)

SZ=schizophrenia; BP=bipolar

The hypothesis that PMD and SAD cases would have a higher proportion of cases who were in a relationship over the follow-up compared with schizophrenia cases was tested. There was evidence that PMD cases were more likely to be in a relationship compared with schizophrenia cases (OR 4.48, 95% CI 2.05-9.77, p<0.001) and that SAD cases were more likely to be in a relationship compared with schizophrenia cases (OR 3.28, 95% CI 1.14-9.44, p=0.028; Table 7-66).

Table 7-66: OR, CI and p value for comparisons between the groups of the main relationship status over the follow-up period

	PMD vs. SZ (n205)	PMD vs. BP (n85)	PMD vs. SAD (n49)	SAD vs. SZ (n188)	SAD vs. BP (n68)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Relationship status – in a relationship	4.48 (2.05-9.77)***	0.98 (0.41-2.36)	1.37 (0.41-4.54)	3.28 (1.14-9.44)**	0.72 (0.23-2.22)

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

There were some differences in the findings based on the baseline diagnosis analyses and lifetime diagnosis analyses. The baseline analyses found evidence that PMD cases were more likely to be in a relationship compared with schizophrenia cases and SAD cases whereas only the PMD group compared with the schizophrenia group not PMD compared with SAD was supported by the lifetime analyses. The baseline analyses supported bipolar cases being more likely to be in a relationship compared with SAD cases whereas the lifetime analyses did not support this. The lifetime diagnosis analyses reveal evidence that SAD cases were more likely to be in a relationship compared with schizophrenia which was not found in the baseline analyses.

7.6.2.2.3. Close confidants by lifetime diagnosis

Table 7-67 shows that PMD cases had the highest percentage of cases with a close confidant at 90%. This was followed by bipolar cases with 70%, SAD cases at 62.5% and schizophrenia cases had the lowest at 50% (number in analyses: 144).

Table 7-67: Comparison of close confidants over follow-up by lifetime diagnosis

	PMD (n20)	**SAD (n8)**	**SZ (n86)**	**BP (n30)**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Close confidant:				
Yes	18 (90.0)	5 (62.5)	43 (50.0)	21 (70.0)
No	2 (10.0)	3 (37.5)	43 (50.0)	9 (30.0)

SZ=schizophrenia; BP=bipolar

The hypothesis that PMD or SAD cases would have a higher proportion of cases with a close confidant over follow-up compared with schizophrenia cases was tested. There was strong evidence that PMD cases were more likely to have a close confidant over the follow-up period compared with schizophrenia cases (OR 9.00, 95% CI 1.97-41.18, p=0.005; Table 7-68). There was no evidence of a difference between SAD and schizophrenia cases (OR 1.67, 95% CI 0.37-7.41, p=0.502), and there was no evidence of any other differences.

The baseline analyses found no difference between any of the groups in terms of close confidants whereas these lifetime analyses found that PMD cases were more likely to have close confidants compared with schizophrenia cases.

Table 7-68: OR, CI and p value for comparisons between the groups of the close confidants variable over the follow-up period

	PMD vs. SZ (n106)	**PMD vs. BP (n50)**	**PMD vs. SAD (n28)**	**SAD vs. SZ (n94)**	**SAD vs. BP (n38)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Close confidants	9.00 (1.97-41.18)***	3.86 (0.74-20.21)	5.40 (0.70-41.75)	1.67 (0.37-7.41)	0.71 (0.14-3.65)

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

7.6.2.2.4. Time in prison by lifetime diagnosis

Table 7-69 shows that schizophrenia cases had the highest percentage of cases who had been to prison over the follow-up (15.3%) and bipolar cases had the lowest (3.7%). PMD and SAD cases were between these with 5.7% and 6.7% respectively. The median number of months in prison was the same for all groups (zero) when all cases were included. However, when only incarcerated cases were included, PMD cases spent longer in prison at 11.5 months. This was followed by the SAD group with five months and finally schizophrenia and bipolar cases both with three months (number in analyses: 274).

The hypothesis that PMD and SAD cases would have a lower proportion of cases who had been in prison over the follow-up compared with schizophrenia cases was tested. There was no evidence that any of the groups differed in terms of having been to prison or not (Table 7-70). There was no evidence of any differences between any of the groups in terms of months in prison when all cases were included. If only cases who had attended prison were included in the analysis, there was evidence that PMD cases spent more time in prison compared with SAD cases (beta coefficient 6.50, 95% CI 0.13 to 12.87, p=0.046) and that SAD cases spent more time in prison compared with bipolar cases (beta coefficient 2.00, 95% CI 0.41 to 3.59, p=0.014). There was also some very weak evidence that PMD cases spent more time in prison compared with bipolar cases (beta coefficient 8.50, 95% CI -1.43 to 18.43, p=0.093).

The findings on time in prison based on the lifetime diagnosis analyses are different from the findings based on the baseline diagnosis analyses. The baseline analyses found evidence that more schizophrenia cases went to prison compared with PMD cases and that PMD cases spent longer in prison when all cases and when only incarcerated cases

were examined, both of which were not supported by the lifetime analyses. When examining time in prison only for cases who went to prison, the baseline analyses found strong evidence that the SAD cases spent more time in prison compared with PMD, whereas this analysis finds evidence of the opposite: that PMD cases spent more time in prison. The baseline diagnosis analyses found evidence that incarcerated SAD cases spent longer in prison compared with incarcerated bipolar cases which is supported by the lifetime diagnosis analyses.

Table 7-69: Comparison of prison contacts by lifetime diagnosis

	PMD (n35)	**SAD (n15)**	**SZ (n170)**	**BP (n54)**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Went to prison: **No** **Yes**	 33 (94.3) 2 (5.7)	 14 (93.3) 1 (6.7)	 144 (84.7) 26 (15.3)	 52 (96.3) 2 (3.7)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Months in prison (for all cases)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Months in prison (for incarcerated cases only)	11.5 (5-18)	5 (5-5)	3 (1-6)	3 (2-4)

SZ=schizophrenia; BP=bipolar; IQR=inter quartile range

Table 7-70: OR, coefficients, CI and p value for comparisons between the groups for time in prison

	PMD vs. SZ (n205)	**PMD vs. BP (n89)**	**PMD vs. SAD (n50)**	**SAD vs. SZ (n185)**	**SAD vs. BP (n69)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Went to prison	0.34 (0.08-1.49)	1.58 (0.21-11.74)	0.85 (0.07-10.14)	0.40 (0.05-3.14)	1.86 (0.16-22.00)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Months in prison (for all cases)	-0.64 (-2.05 to 0.76)	0.55 (-0.52 to 1.61)	0.32 (-1.02 to 1.67)	-0.97 (-2.12 to 0.18)	0.22 (-0.46 to 0.91)
Months in prison (for incarcerated cases only)	3.00 (-7.86 to 13.86)	8.50 (-1.43 to 18.43)*	6.50 (0.13 to 12.87)**	-3.50 (-9.20 to 2.20)	2.00 (0.41 to 3.59)**

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

The baseline analyses found that incarcerated SAD cases spent more time in prison compared with incarcerated schizophrenia cases which was not supported by the lifetime analyses. There was some weak evidence from the lifetime analyses that

incarcerated PMD cases were more likely to spend longer in prison compared with incarcerated bipolar cases which was not supported by the baseline analyses.

7.6.2.2.5. Social outcomes summary by lifetime diagnosis

The baseline and lifetime diagnosis analyses found the same differences between the groups in terms of social outcomes of employment status. However, there were some differences in findings in time in prison, relationship status and close confidants. One of the major changes is in the comparisons between PMD and schizophrenia cases. The baseline analyses found that schizophrenia cases were more likely to go to prison over the follow-up and spent longer time in prison whereas there was no evidence of this from the lifetime diagnosis analyses. The lifetime diagnosis analyses found evidence that PMD cases were more likely to have a close confidant at follow-up whereas the baseline analyses found no such evidence.

There were also some differences in the comparisons between PMD and SAD cases. The baseline analyses found evidence that PMD cases were more likely to be in a relationship over the follow-up compared with SAD cases but this was not supported by the lifetime analyses. The baseline analyses also found evidence that incarcerated SAD cases spent more time in prison compared with PMD incarcerated cases. However, the lifetime analyses found the opposite with incarcerated PMD cases spending more time in prison. There were a few other minor differences with findings on SAD, bipolar and schizophrenia cases.

7.6.3. Service use over 10 years by lifetime diagnosis

7.6.3.1. Binary hospitalisation by lifetime diagnosis

Table 7-71 shows that PMD cases had the highest percentage of cases who were not admitted over the follow-up period with 20.9%. This was closely followed by SAD cases with 18.8%. Schizophrenia and bipolar cases had the lowest percentage of cases who were never admitted with 7.1% and 4.8% respectively (number in analyses: 317).

Table 7-71: Comparison of hospitalisation data by lifetime diagnosis

	PMD (n43)	**SAD (n16)**	**SZ (n196)**	**Mania (n62)**
	N (%)	**N (%)**	**N (%)**	**N (%)**
Hospitalised:				
No admission	9 (20.9)	3 (18.8)	14 (7.1)	3 (4.8)
Admission	34 (79.1)	13 (81.3)	182 (92.9)	59 (95.2)

SZ=schizophrenia; BP=bipolar

The hypothesis that PMD and SAD cases would have a lower proportion of cases admitted compared with schizophrenia cases was tested. There was evidence that PMD cases were less likely to be admitted over the follow-up compared with schizophrenia cases (OR 0.29, 95% CI 0.12-0.72, p=0.008) but there was no evidence of a difference between SAD and schizophrenia cases (OR 0.33, 95% CI 0.08-1.31, p=0.115) There was evidence that PMD cases were less likely to be admitted over the follow-up compared with bipolar cases (OR 0.19, 95% CI 0.05-0.76, p=0.019; Table 7-72) and there was some weak evidence that SAD cases were less likely to be admitted compared with bipolar cases (OR 0.22, 95% CI 0.04-1.22, p=0.083).

Table 7-72: OR, CI and p value for comparisons between the groups on hospitalisation

	PMD vs. SZ (n239)	**PMD vs. BP (n105)**	**PMD vs. SAD (n59)**	**SAD vs. SZ (n212)**	**SAD vs. BP (n78)**
	OR (CI)	**OR (CI)**	**OR (CI)**	**OR (CI)**	**OR (CI)**
Hospitalisation	0.29 (0.12-0.72)***	0.19 (0.05-0.76)**	0.87 (0.20-3.73)	0.33 (0.08-1.31)	0.22 (0.04-1.22)*

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

The finding based on the baseline diagnoses that PMD cases were less likely to be admitted compared with bipolar cases was supported by the lifetime diagnosis analyses. However, the lifetime analyses finding that PMD cases were less likely to be admitted compared with schizophrenia cases was not found based on the baseline analyses. The weak finding based on the lifetime diagnoses that SAD cases were less likely to be admitted compared with bipolar cases was not found based on the baseline analyses.

7.6.3.2. Total number of hospitalisations by lifetime diagnosis

The results based on the lifetime diagnoses were the same as the results based on the baseline diagnoses except the weak finding that SAD cases had a lower rate of admissions compared to schizophrenia was no longer supported (Appendix A).

7.6.3.3. Total number of days hospitalised by lifetime diagnosis

There were no differences in the findings on total number of days hospitalised between the baseline and lifetime diagnosis analyses (Appendix A). Both sets of analyses found evidence that PMD cases had less days hospitalised compared with schizophrenia cases.

7.6.3.4. Percentage of the follow-up spent as an inpatient by lifetime diagnosis

There were no differences in the findings on the percentage of the follow-up spent as an inpatient between the baseline and lifetime diagnosis analyses (Appendix A).

7.6.3.5. Percentage of admissions which were compulsory by lifetime diagnosis

Table 7-73 shows that PMD cases had the highest median percentage of compulsory admissions with 88.9%, SAD had the lowest with 25%, and the schizophrenia and bipolar cases scored between these two with 75% and 69.7% respectively (number in analyses: 205).

Table 7-73: Comparison of percentage of hospitalisations which were compulsory data by lifetime diagnosis

	PMD (n25)	SAD (n7)	SZ (n125)	BP (n48)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Percentage of admissions compulsory	88.9 (0-100)	25 (0-100)	75 (25-100)	69.7 (33.3-100)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

The hypothesis that PMD and SAD cases would have a lower proportion of cases being compulsorily admitted compared with schizophrenia cases was tested. There was no evidence to support this hypothesis and there was no evidence of any other differences between any of the groups (Table 7-74).

Table 7-74: Coefficient, CI and p value for comparisons between the groups of the percentage of hospitalisations which were compulsory over the follow-up period

	PMD vs. SZ (n150)	PMD vs. BP (n73)	PMD vs. SAD (n32)	SAD vs. SZ (n132)	SAD vs. BP (n55)
	Beta coefficient (CI)	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**	**Beta coefficient (CI)**
Percentage of admissions compulsory	-5.64 (-25.53 to 14.25)	-6.28 (-27.93 to 15.37)	17.64 (-19.55 to 54.83)	-23.28 (-57.06 to 10.50)	-23.92 (-58.96 to 11.12)

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

These findings, based on the lifetime diagnoses, that there are no differences between the groups are different from those based on the baseline diagnoses. The baseline analyses found evidence that PMD cases had a lower percentage of compulsory admissions compared with schizophrenia and bipolar cases, and weak evidence that SAD cases had a lower percentage of compulsory admissions compared with schizophrenia and bipolar cases.

7.6.3.6. Having ever been admitted compulsorily by lifetime diagnosis

There were no differences in the findings on having ever been admitted compulsorily between the baseline and lifetime diagnosis analyses (Appendix A).

7.6.3.7. Percentage of hospitalisations involving the police by lifetime diagnosis

There were no differences in the findings on percentage of hospitalisations involving the police between the baseline and lifetime diagnosis analyses (Appendix A).

7.6.3.8. Summary of service use by lifetime diagnosis

Both baseline and lifetime diagnoses found evidence of the same differences between the groups in the following variables: total number of hospitalisations; total number of days hospitalised; percentage of the follow-up as an inpatient; having ever been admitted compulsorily; and percentage of hospitalisations involving the police. There were differences, however, in two service use outcomes: binary hospitalisations; and percentage of admissions which were compulsory.

Binary hospitalisations based on the baseline analyses only found weak evidence of a difference between PMD and bipolar cases whereas lifetime diagnoses found evidence of differences between bipolar and PMD cases, PMD and schizophrenia cases and weak evidence of a difference between bipolar and SAD cases. The findings on the percentage of compulsory admissions from the baseline analyses that there was a difference between schizophrenia and PMD cases, PMD and bipolar cases, and SAD and bipolar cases was not supported by the lifetime diagnosis analyses.

7.7. Overall summary of the chapter

There are some important differences in findings when analyses are based on lifetime diagnoses compared with baseline diagnoses. One of these is that the lifetime diagnoses analyses identified PMD cases to be more likely to attempt suicide compared with schizophrenia cases. This was not identified by the baseline diagnosis analyses. There were also some differences between PMD and SAD cases identified by the lifetime

diagnosis analyses. These were that PMD cases had better outcomes on a number of course of illness outcomes, which were not identified by the baseline analyses.

CHAPTER 8. Discussion

"If science proves some belief of Buddhism wrong, then Buddhism will have to change"[439]

Tenzin Gyatso, 14th Dalai Lama (2005)

8.1. Aims of the chapter

The aim of this chapter was to summarise the main findings, as well as to reflect on the limitations of the thesis and evaluate the findings in light of these limitations. The theoretical and clinical implications of the study are then discussed. This was done for the case control and cohort study separately as they addressed different questions and have different limitations associated with each. Finally, future research and final conclusions are considered.

8.2. Risk factors

8.2.1. Summary of results

8.2.1.1. Hypotheses

In this thesis, I set out to test a number of hypotheses about psychosocial risk factors, PMD and SAD. The following hypotheses were supported by the results:

- PMD would be associated with being of non-white British ethnicity (Asian and 'other' ethnicity).
- SAD would be associated with being of non-white British ethnicity (Black African and African Caribbean).
- PMD would be associated with being born outside the UK.
- Lower educational attainment would be more frequent in PMD cases compared with controls.
- Unemployment would be more frequent in PMD and SAD cases compared with controls.

- Factors associated with social isolation, such as living situation, relationship status and contact with friends, would be more frequent in PMD and SAD cases compared with controls.
- Childhood adversity would be more frequent in PMD cases compared with controls.
- Independent life events would be more frequent in PMD cases in the year prior to illness onset compared with controls.

The following hypotheses were not supported by the results:

- SAD would be associated with being born outside the UK.
- PMD would be associated with being older (actually associated with being younger), with being female (no association) and being in the London site (no association).
- SAD would be associated with being older (actually associated with being younger), with being female (actually associated with males) and being in the London site (no association).
- Lower educational attainment would be more frequent in SAD cases compared with controls (no association).
- Childhood adversity would be more frequent in SAD cases compared with controls (no association).

The following hypotheses were unclear:

- Independent life events would be more frequent in SAD cases in the year prior to illness onset compared with controls (no association).

8.2.1.2. Exploratory analysis of life events

The exploratory analysis of the life events data showed evidence that PMD cases had the highest increased odds of having experienced both a life event and a life difficulty. There was evidence that schizophrenia cases had the highest increased odds of having experienced either a life event or a life difficulty. Both of these findings were supported by both the baseline and lifetime diagnosis analyses.

There was evidence from the baseline and lifetime analyses that humiliation life difficulties were associated with an increased odds of PMD, SAD (lifetime analyses not available), schizophrenia and bipolar disorder. This was supported by both the baseline and life time diagnosis analyses.

The exploration of humiliation events showed evidence of a strong link between PMD and humiliation life events as large odds ratios were reported and a temporal relationship was identified with larger odds ratios the closer to the onset of an event. This was supported by both the baseline and lifetime diagnosis analyses. This was the same for SAD cases but only for the baseline analyses. There was no evidence of a link between humiliation life events and bipolar disorder based on the baseline diagnoses but there was evidence of a link when based on the lifetime diagnoses. There was only very weak evidence of a link between humiliation life events and schizophrenia based on baseline and lifetime diagnosis analyses.

Before going on to interpret the results, the methodological limitations of the study are examined.

8.2.2. Methodological considerations

Consideration of the methodological limitations of epidemiological studies involves considering whether the observed association between an exposure and an outcome could be the result of: bias; chance; or confounding.[424] These will now be discussed along with other key methodological considerations which are causality, study specific limitations and strengths.

8.2.2.1. Bias

Hennekens and Buring defined bias as "...any systematic error in an epidemiological study that results in an incorrect estimate of the association between exposure and odds of disease".[424] Of course bias is possible in any research study, but with epidemiological studies it is the effect of bias on the observed relationship between exposure and outcome which is of importance. Bias can be broken down into selection bias and information bias.

8.2.2.1.1. Selection bias

Selection bias has been defined as any error that arises in the process of identifying the study population.[424] Specifically within case control studies, like this one, this is when the inclusion of subjects into the study on the basis of outcome is dependent on exposure. Within this study selection bias could exist in three ways. Firstly, although the study population is described as an incidence sample, it is actually a help-seeking incidence sample. All new cases of psychosis who present to secondary services within a defined area were included. Therefore cases who may have newly developed psychosis but have not approached services would have been missed. There is also the possibility that not all cases who presented to services were successfully identified and included. There is the possibility that cases who have experienced some of the risk

factors that have been examined in this thesis are more likely to seek help. For example, cases who have experienced childhood adversity may have had more contact with health and social care services during childhood which may increase their probability of approaching services when problems develop in adulthood. This kind of bias could lead to an over estimation of childhood adversity in the psychosis cases. Similarly, cases with a family history of mental illness could have witnessed family members being sectioned and be less likely to seek help for mental health issues and those with social isolation may be less likely to come into contact with services as they have no friends or family to bring them to the attention of services. Both of these would lead to an underestimation of the association between these exposures and the outcome of having psychosis.

A second form of selection bias comes from the interview status. Although all incidence cases were included in the study overall, only a proportion of these cases were interviewed. Of those interviewed, there was much missing data for the key risk factors being examined in this thesis, including childhood adversity and especially life events; those with missing data are, in effect, not selected into analyses. There were significant differences in missing data between cases and controls as would be expected due to the nature of the study but there were also significant differences between diagnostic groups in terms of family history, childhood adversity and a few indicators of social isolation. This could have led to selection bias.

Finally, consideration of selection bias resulting in the differential recruitment of cases and controls must be considered. A random sample of controls matched by geographic location were recruited making the control sample comparable to the cases as this was considered the best way to get comparable controls. However, there is still the potential

for bias as controls are volunteers and not all who are approached, even if selected randomly, will agree to take part. Those who agree to participate may differ from those who do not on important characteristics. However, it is not possible to assess this but it must be borne in mind as a potential source of bias. Controls were examined to make sure they did not meet criteria to be a case. As mentioned, the selection of incidence cases through mental health services was biased in that it selected only those who came into contact with services. However, the alternative of interviewing all residents in the catchment area was beyond the scope of this thesis.

8.2.2.1.2. Information Bias

Information bias results when there are systematic differences in the way that data on exposure and/or outcome are obtained from each group within the study.[424] This can lead to inaccurate results. Information bias can come in three forms, recall bias, interviewer bias and misclassification bias.[424]

Recall bias occurs when a particular study group recall experiences differently from other study groups and is a particular problem for case control studies.[424] This is a significant issue within this thesis. Cases may tend to want to find an explanation for their illness and therefore may scrutinize their memory for past exposure more intensively compared with controls.[160] This will lead to recall bias in estimates of association between exposure and disease. The disorder under investigation may also lead to bias by impairing the amount and accuracy of information provided.[160] Within this thesis, comparing between different diagnoses may also lead to differences in findings as a result of differing function of illness between diagnoses rather than as a true difference between diagnoses. For example, schizophrenia is associated with cognitive deficits and memory problems.[440] This could lead to an under reporting of risk

factors such as life events and childhood adversity, and therefore an underestimation of the association between childhood adversity and schizophrenia. Depression is associated with high levels of rumination[441] (rumination is also a feature of PMD[442]). This rumination could relate to previous experiences and could result in cases looking for explanations of their current mental health and experiences. This could give rise to PMD cases being more likely to recall childhood adversity and could therefore lead to an overestimation of the association between childhood adversity and PMD. This is a potential alternative explanation for the findings from this thesis that life events and difficulties, and childhood adversity is associated with PMD. The finding of a temporal relationship in life events in the PMD cases, with higher odds ratios at time periods closer to onset could be a result of recall of life events being higher closer to interview.

Interviewer bias occurs when there is a systematic difference between study groups in the eliciting, recording or interpreting of information from participants.[424] Interviewer bias is a particular problem in case control studies in relation to exposure status as knowledge of the participant's outcome status may lead to differential probing in the exposure history.[160, 424] Interviewer bias could have occurred within this thesis as case and control status at baseline was clearly known by interviewers collecting data on exposure. This could have lead to differential questioning and probing of cases about their exposure in these areas. It was not possible to assess the extent of interviewer bias in this study and so must be borne in mind as a limitation. One way to overcome this issue in future studies could be to have interviewers examining exposure status blind to case control status, although this would be very hard to implement, especially as many cases were interviewed within a mental health setting.

Data collection methods were based on patient interview and self report as well as clinical records. Interviews were based on standardised, established questionnaires and were conducted by trained interviewers and were administered to cases and controls in the same way. This is likely to reduce the potential for bias. The combination of data collection via interview and notes is likely to have reduced bias in cases. However, clinical records were not available for controls and therefore, this strength could have become a source of bias, also as there was a difference in the method of exposure assessment between cases and controls. Also, information from case notes could be biased as they are dependent on what and how clinicians decide to record and inaccuracies are possible. As previously mentioned, blinding of study interviewers was not possible within the context of this study. Further to this, the context in which the interview is conducted can affect the responses given.[160] As cases and controls were generally interviewed in differing locations (cases mostly in mental health settings and controls mostly in their own home), this could lead to a systematic bias between cases and controls.

Misclassification bias is when participants are erroneously categorized into exposure or outcome groups[424] and can be an alternative explanation for an observed association between an exposure and an outcome.[160] Random misclassification is present in almost all types of epidemiological studies and will lead to a dilution of any true associations between exposures and outcomes. Bromet et al.[160] highlighted that differential misclassification of exposure can lead to a masking or attenuating of an association. For example, if cases are unwilling to report past exposures that they may blame themselves for, e.g. life events or childhood adversity, but controls are not, this could lead to a masking of a true association. [160] In case control studies which use self-reported exposure, systematic misclassification bias is a potential serious problem, which can

lead to an overestimation or underestimation of the true association between exposure and outcome.[424] Within this study, the majority of exposures examined were measured through participant self-report and/or clinical notes, both of which are potentially subject to misclassification bias. Unfortunately, misclassification bias is incredibly difficult to assess and thus, its effect within this thesis was not measureable.

8.2.2.1.3. Bias conclusions

As demonstrated in this section, there are many potential sources of bias in this study and Ioannidis points out that "...with increasing bias, the chances that a research finding is true diminish considerably".[443] Hennekens and Buring point out that unlike chance and confounding, bias cannot be measured quantitatively and therefore the role of bias as an alternative explanation of an observed association must be considered in the interpretation of results.[424]

8.2.2.2. Chance

Chance has been described by Ioannidis as: "...variability that causes some findings to be false by chance even though the study design, data, analysis and presentation are perfect."[443] There are three main issues to think about in the context of chance: interpretation of the p value and confidence interval; clinical versus statistical significance; and multiple testing.

8.2.2.2.1. Interpretation of the p value and confidence interval

Inference is a generalisation about a larger group based on a subset of those individuals.[424] This is necessary within research as it is not normally possible to conduct research on an entire population, so samples of that population are used on which to

base inferences. When inferences are made, there is the potential that the inference will be imprecise or inaccurate as a result of chance or sampling variability.[424] Therefore, hypothesis testing is needed to examine the degree to which sampling variability may account for the observed results. The hypothesis testing statistic is simply a test of the difference between the study finding and the findings that would be expected if the null hypothesis were true.[424] The p value associated with the test statistic indicates the probability of obtaining the result, if the null hypothesis were true. The p value is usually set at 0.05 by convention, and at this level means that there is a 1 in 20 probability of observing the finding as a result of chance alone.[424, 444] However, within this thesis a p-value of 0.1 has been taken to indicate weak evidence of an association, 0.5 to indicate moderate evidence and 0.01 to indicate strong evidence. This was to ensure no potential effects were missed due to a lack of power. Therefore, one in ten findings are likely to be due to chance.

As the p value is a function of the size of the difference between two groups (or the strength of an association) and the sample size, then small (but relatively trivial) effect sizes may become statistically significant due to large sample sizes.[444] Hence, Hennekens and Buring recommend that p values should be used as a guide only, and using the confidence interval surrounding the effect size to supplement this information. The confidence interval represents the likely range within which the true value lies, therefore the 95% confidence interval means that we can be 95% sure that the true effect size lies somewhere within the confidence interval range. Confidence intervals indicate the amount of variability in the estimate of the effect size. Wide confidence intervals indicate less precise estimates of the effect size and vice versa. Hennekens and Buring[424] suggest that confidence intervals are particularly important when interpreting null findings as a narrow confidence interval and a non-significant p value support the

conclusion that the null hypothesis is true while a wide confidence interval and non-significant p value indicate that the sample size may have been too small to detect a difference between groups.

As a result of these two issues, both the p values and confidence intervals must be examined when interpreting the results of a study. Some of the findings for the SAD risk factors analyses have significant p values but very large confidence intervals demonstrating imprecise estimates of the effect sizes, therefore these results must be interpreted with caution. Some other findings reveal an effect size, similar or larger to effect sizes in other diagnostic groups which were statistically significant, but the confidence interval was wide and the effect size in the SAD group was not statistically significant. Therefore, rejecting the alternative hypothesis tied with these results must be done with caution. One way to avoid lack of power leading to false negatives is to conduct power calculations. A power calculation was conducted within this thesis which indicated that there was sufficient power to identify moderate effects in the PMD group. However, this was an exploratory study of a large number of risk factors and outcomes in PMD and SAD, and power calculations were not conducted for all analyses. Additionally, due to the nature of this study (incidence sample), it was not possible to control the numbers recruited into the study other than by extending the recruitment period or extending the recruitment geographical locations, and to get enough SAD cases would take an extreme amount of extra resources as SAD is a very rare diagnosis. Additionally, the majority of the data had already been collected at the start of this thesis, thus recruiting more cases was not possible. In light of all these issues, it is most appropriate to say that due to low numbers and a lack of power, the findings on risk factors in SAD cases are inconclusive.

This issue of power is also relevant to the differences in findings between the baseline and lifetime diagnoses. The baseline analyses showed evidence that the following risk factors were associated with an increased odds of PMD compared with controls, but this was not supported by the life time diagnoses: being older; having not been born in the UK; never having had a long term relationship; and having contact with family less than monthly. This difference could be due to the lower numbers in the PMD group in the lifetime diagnosis analyses compared with the numbers in the PMD group in the baseline diagnosis analyses, and thus lower power.

8.2.2.2.2. Clinical versus statistical significance

As discussed above, even the smallest of differences between groups may reach statistical significance if the sample size is sufficiently large.[424] Therefore, it is important to distinguish between statistically significant findings and clinically significant findings.[444] This issue is discussed in relation to this thesis in section 8.2.2.2.4 below.

8.2.2.2.3. Multiple testing

Within epidemiological studies, it is common to test the effect of a large number of risk factors on outcomes. However, Hennekens and Buring[424] state that as the number of variables tested increases, so does the likelihood of finding a statistically significant difference due to chance. Within the risk factors results chapter, as more than 10 tests were conducted but a p value threshold of 0.1 was used, it is likely that at least one false positive finding is present. As it is impossible to determine which findings are the ones due to chance, this will simply have to remain a major limitation of the thesis. It is important to be conscious that there are likely to be spurious findings.

8.2.2.2.4. Chance conclusions

This section has demonstrated that when interpreting results, it is vital to examine the effect size, the confidence interval, and the p value associated with the test statistic. An important message to take away from this discussion of chance especially in relation to the SAD analyses, is that "Absence of evidence is not evidence of absence."[444]

Bearing in mind the issues discussed in this section, the finding in the adjusted analyses that a lifetime diagnosis of PMD is associated with presence of childhood adversity and the number of different types of childhood adversity need to be re-evaluated. For presence of childhood adversity, the OR was 2.57 and the CI 1.02-6.44. Although this finding is statistically significant at the p value threshold of 0.05, the reasonably wide confidence interval indicates a less precise estimate of the effect.

8.2.2.3. Confounding

Confounding has been described as the possibility that an observed association between an exposure and an outcome is due, either completely or in part, to factors other than those under investigation.[424] Confounders must be associated with the exposure and, independently, with the outcome. It is introduced not by the investigator or participant as in the case of bias, but is a function of the complex interrelationship between various exposures and outcomes.[424] Confounding can lead to either an overestimation or underestimation of the true relationship between exposures and diseases and can even change the direction of the observed effect.[424] Confounding is a potential problem in all studies and must always be considered as an alternative explanation for study findings, particularly in observational case-control and cohort designs.[424] There are key components that a confounder must be to qualify as such. These are: the potential confounder must be independently associated with the outcome of interest, but the

association need not be causal; the confounder cannot be related to risk of disease only through its association with the exposure (thus, there must be an association between the confounder and disease even among non-exposed individuals); and the confounder cannot only be an intermediate link in the causal chain between the exposure and disease under investigation.[424]

There are various methods to control for the effects of confounding which fall under design stage methods (randomisation, restriction and matching) and analysis stage methods (stratification and multivariable analyses). Multivariable analyses were used in this thesis as it allows for efficient estimation by controlling for multiple confounders simultaneously.[424] Using multivariable analyses, the degree of confounding within a study is investigated by examining the difference between the crude and adjusted estimates.[424] Within this thesis, adjustment for key demographic variables (age, centre, gender and ethnicity) was conducted. Due to low numbers, it was not sensible to control for other factors as this would seriously reduce the power of the analyses. However, it is possible that interactions exist among some of the variables which would require adjustment for each other, e.g. childhood adversity has been found to be associated with life events.[118-120] This is something that would best be examined in another study with a larger sample size.

A further major issue with confounders is that only confounders that have been measured can be adjusted for.[445] However, there is nothing that can be done about unmeasured confounders other than to consider what they might be and appraise how they might have influenced the findings. Within this thesis, there are a huge number of unmeasured confounding variables, such as obstetric complications and cannabis use, and this must be borne in mind as a limitation.

8.2.2.4. Causality

Schwartz & Susser stress that "…causation is not directly observable; it can only be inferred."[446] Bradford Hill[447] has described what aspects of association should be considered before coming to a conclusion of causation. This was in relation to occupational medicine but is now more widely applied to many branches of medicine and science more widely. These aspects include: strength (the strength of the association must be large); consistency (repeated observation of the association in different samples, places, circumstances and times); specificity (no association with the exposure and outcomes other than the one under investigation); temporality (the exposure must precede the outcome); biological gradient (a dose response curve is present); plausibility (the association is biologically plausible); coherence (the association should not contradict what is already 'known'); experiment (experimental data supports the causal hypothesis); and analogy (making inferences based in similar circumstances observed elsewhere).[447]

One of the key criteria is temporality. Bromet et al. point out that in a case-control study "the exposure may plausibly be a consequence rather than a cause of the disease".[160] Morgan et al.[448] highlight that studying social factors in psychosis is difficult as the development of psychosis is frequently preceded or accompanied by a decline in social functioning (loss of employment, disintegration of social networks and downward social mobility). This makes it unclear whether social experience is a cause or consequence of the developing psychosis. This is discussed further in section 8.2.2.5 below.

Of the other criteria, this thesis is unable to demonstrate consistency and coherence as no study has examined these risk factors in PMD cases previously. However, analogy is possible as these risk factors have been found to be associated with similar disorders

(see chapter 3), however, for this same reason specificity cannot be demonstrated as the risk factor of childhood adversity has been shown to be associated with other disorders (see chapter 3). Experimental data would not be ethical within the context of this thesis. A biological gradient is reported in the form of a linear association with number of childhood adversity factors but the strength of the effect size is small. The plausibility of the findings are good because disorders similar to PMD and SAD (schizophrenia and non-psychotic depression) have been associated with the same social risk factors (see chapter 3). In view of the fact that this thesis can only demonstrate a small number of the criteria, it should be borne in mind that Bradford Hill[447] stated that no single one of these items can prove or disprove causality, but they can support the hypothesis of causality.

8.2.2.5. Study specific limitations

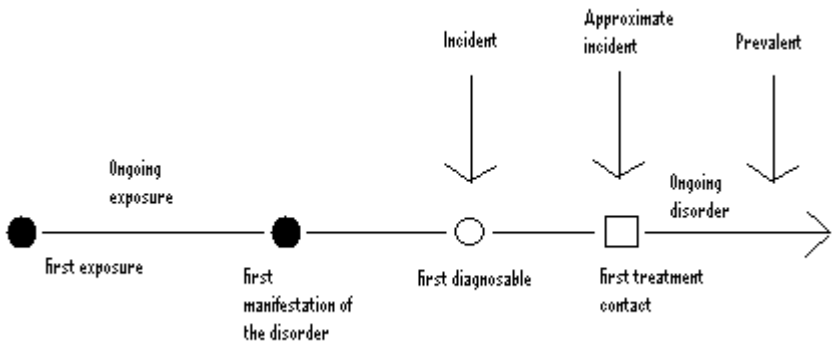
As well as limitations specific to epidemiological studies, this thesis was also subject to more specific limitations. One fundamental issue is diagnostic classification. This is a version of misclassification bias but is discussed here as it is a particular problem for psychiatric studies due to issues discussed in Chapter 2, and must also be borne in mind when interpreting the findings. Briefly, psychiatric classification differs from other 'disorders' as there are no objective measures and a set of descriptive diagnoses must be used. Blurred sets of symptoms are used, not distinct typologies; therefore the results based on these classifications will also be blurred, leading to inaccurate and possibly completely wrong findings. A further complication with mental health research is co-morbidity of psychiatric diagnoses,[446] something which has not been examined or accounted for in this thesis.

Morgan et al.[448] point out some limitations with research on social processes as aetiological factors in psychosis including that epidemiological research often uses crude dichotomies, e.g. urban versus rural. This means that "the precise meaning of observed associations is unclear, and the social experiences that these variables may index remain unknown".[448] This is certainly true in this thesis with dichotomies such as abused versus not abused and experienced life event versus no life event experiences. However, within this thesis, variable categories were grouped into smaller number of categories (binary where possible) for clarity and to increase power.

In terms of limitations of specific measures, there have been some criticisms of the LEDS. Dohrenwend et al.[415] state that although the LEDS is based on a contextual approach and is therefore more precise than the previous approaches (namely the checklist approaches) the LEDS is also more 'gross' as it involves collapsing down the events, the social situation of the events and the personal history of the person involved into a single measure, in non-specific ways. This results in the inability to distinguish which of the components are salient in the research finding. However, Brown and Harris[132] point out that there are no satisfactory alternatives as all the alternatives have more serious methodological limitations.

There are also methodological issues, which are specific to studying psychosis cases. The first relates to incidence. Within this thesis, the aim was to examine risk factors and outcomes based on the study of incidence cases, i.e. new cases of the disorder. What we have actually examined is cases with a first contact with secondary treatment services. This is represented in figure 8-1. This means that cases who have low level psychosis and are being managed by a general practitioner or who never present to services are being missed. Thus, perhaps sampling from what are in effect administrative incidence

cases leads to an oversampling from more unwell cases. The second specific issue is that psychosis cases often have prodromal periods and long durations of untreated psychosis (figure 8-1). This makes the date of onset very difficult to pinpoint. Hafner et al.[449] stated that in such cases, the time between the true onset and the recruitment into the study is important in interpreting the results. In the context of the risk factor findings in this thesis, this delay between onset and first contact with services means that the temporal ordering of risk factors is difficult. This is reflected by the fact that the number of cases with data on life events in the year preceding onset is low as it cannot be accurately done for many cases due to long duration of untreated psychosis. Prodromal symptoms can also be a problem as premorbid signs and symptoms might in fact generate the exposure being investigated.[160]



(From Bromet et al., 2006[160])

Figure 8-1: Temporal order in case-control studies

Ioannidis states that "most published research findings are false" due to a combination of factors including: flexibility in designs, definitions, outcomes and analytic modes; lack of adherence to common standards; and financial and other interests and prejudices within a scientific field.[443] In light of these methodological limitations, in relation to epidemiological studies, Ioannidis state that "Epidemiological studies of an exploratory nature perform even worse [than other types of studies], especially when underpowered,

but even well-powered epidemiological studies may have only a one in five chance of being true...".[443] This is worth considering in the interpretation of the results.

A further methodological limitation is the exclusion of over 65 year olds. Due to the data available, only cases aged 16-65 were included in this thesis. This was because the original study aimed to examine an incidence sample of adults with psychosis. Over 65 year olds were excluded as they are classed as an elderly population and this was not the aim of the original study, and resources did not allow recruitment from geriatric services as well as general adult mental health services.

However, a review by Smith et al.[68] has highlighted that in clinical samples, the prevalence of PMD increases with age, although in general population samples there been appears to be no difference in prevalence of PMD across age groups. However, in a more recent study, Crebbin et al.[1] compared PMD and schizophrenia in a sample of 16 year old plus incident psychosis cases. They reported that of the 105 new cases of PMD over 7 years, 31 cases (30%) were aged 65 years or older. Hence, approximately 30% of PMD cases could have been missed due to the age limits. Therefore, all the findings within this thesis may not be valid for PMD geriatric cases. This warrants further research.

8.2.2.6. Methodological strengths

While the methodological limitations listed above are substantial, there are also a number of methodological strengths which improve on previous research and thus can increase our confidence in the findings. The most significant of these is the accounting for diagnostic change. This thesis was based on an incidence sample, and most incidence studies which examine risk factors for disorder in psychiatry base their

analysis on initial diagnosis. However, as shown in chapter 4 and chapter 7, diagnostic stability is not high in psychosis cases and is especially low in diagnoses other than schizophrenia and bipolar disorder. In fact, Schwartz et al. stated that "… the psychiatric diagnoses people receive at the time of onset are often inaccurate. Longitudinal observation tends to clarify the nature of the patient's illness".[160] This thesis has examined initial diagnosis but also lifetime diagnosis based on eight years plus of clinical information to get a more stable, and arguably, more accurate diagnosis. The analyses based on the baseline and lifetime diagnosis showed very similar results with the exception of childhood adversity. Childhood adversity was not significantly associated with a diagnosis of PMD at baseline, but it was significantly associated with a lifetime diagnosis of PMD. Childhood adversity may well have been undermined as a risk factor for PMD if only the baseline diagnosis had been used and an important finding missed.

A further important methodological strength is having included a sample of all first episode cases presenting to services (not just inpatients as is often done). Chapter 4 highlighted the importance of focussing on incident cases rather than prevalence cases as prevalence sampling increases the likelihood of sampling from a more severely ill population. This makes incidence samples preferable and is a strength of this thesis as a more accurate account of risk factors is gained.

Other strengths of the methodology are having a research diagnosis (not just a diagnosis taken from the clinical notes) made by consensus, by a team of researchers and clinicians who were blind to ethnicity. Each part of this diagnosis process is a way of combating bias. Objective diagnosis based only on symptomology and sticking to the exact criteria set down in the ICD-10, rather than using clinical discretion and

judgement in making a diagnosis minimises the risk of bias and cultural interpretation (but does not rule it out).

Perhaps the most important strength of this thesis is that although the results on risk factors in PMD and SAD have a number of methodological limitations, this is the only study that has examined risk factors associated with PMD and SAD, and as such, is a foundation on which to build and to inform for future in the area.

8.2.3. Interpretation of the results

Despite the methodological limitations of this study, the results are very informative.

8.2.3.1. Generic risk factors

The results showed that there was some evidence, be it from baseline or lifetime diagnoses, from the unadjusted or adjusted analyses, that most of the psychosocial risk factors were associated with all of the diagnoses (see Table 8-1). This shows a lack of specificity between the psychosocial risk factors examined here and PMD and SAD, thus suggesting these factors represent risks for psychosis in general or perhaps for mental illness in general. This lack of specificity could be due to several factors. The factors may have been measured too crudely (e.g. it may be the impact of unemployment rather than unemployment itself that is important), or the factors are interacting with other factors that dictate specificity (e.g. genetic risk via specific genes).

However, the exploratory analyses of life events and difficulties indicate that there may be PMD and SAD specific risk factors in specific subtypes of life events and difficulties. This finding warrants further research.

Table 8-1: Overview of psychosocial risk factors and evidence of an association with each diagnostic group

Predictors	PMD	SAD	Schizophrenia	Bipolar
Younger	x	x	x	x
Study centre: London			x	x
Gender: Male		x	x	
Ethnicity:				
White British				
African-Caribbean		x	x	x
Black African		x	x	x
White Other				
Asian (all)	x		x	x
Other	x		x	x
Place of birth: Non-UK	x		x	
Relationship Status: Single	x	x	x	x
Ever had a long term relationship: No	x	x	x	x
Living with: Alone	x	x	x	x
Level of Education:				
Further			x	
School	x		x	
Employment Status: Unemployed	x	x	x	x
Ever worked: No	x (reverse)		x	x
Contact with friends: Never / less than monthly	x		x	x
Contact with family: Never / less than monthly	x	x	x	
Close confidants: No	x	x	x	x
Family history of any mental illness: Yes	x	x	x	x
Family history of psychosis: Yes	x	x	x	x
Parental history of any mental illness: Yes	x	x	x	x
Parental history of psychosis: Yes	x	x	x	x
Life Events: Yes	x	?		x
Life Difficulties: Yes	x	?	x	x
Childhood Adversity: Yes	x		x	x
Number of Childhood Adversity Factors	x	x (reverse)	x	x

8.2.3.2. Differences between baseline and lifetime analyses

There were some important differences between the baseline and lifetime analyses. For example, in the baseline analyses, there was evidence that childhood adversity was associated with increased odds of schizophrenia only. However, based on the lifetime analyses, there was evidence that childhood adversity was associated with increased odds of schizophrenia and PMD.

Differences in findings between baseline and lifetime diagnoses could be due to a number of reasons. Firstly, as the numbers in the lifetime analyses were lower, differences could be due to reduced power in being able to detect effects. This is a

salient point for analyses based on SAD cases as the numbers in some of the analyses were very small. Alternatively, differences could be due to changes in diagnosis.

As the baseline and lifetime diagnoses reveal slightly different results in the risk factors analysis, an important question to be asked could be "which diagnosis is correct?" or "which diagnosis is better?". There are limitations with using the baseline and lifetime diagnoses. As mentioned in Chapter 2, diagnostic classification systems are flawed and thus any analyses based on these diagnoses are flawed. Specifically, the baseline diagnosis has the limitation that in PMD and SAD cases, it is likely to change. This could be due to the fact that it is based on information from a limited period and thus diagnoses are inaccurate, or it could be that the disorder is actually evolving into another psychotic disorder. The lifetime diagnosis has the limitation that it is based on information over a long period of time, thus as diagnosis changes, risk factors measured at baseline may have also changed. Based on all these issues, it is clear that one is not better than the other, they are simply different and yield different results in the risk factors analysis, and until a more reliable diagnostic system is in place, our conclusions are limited.

8.2.3.3. SAD cases

The numbers of SAD cases were small making interpretation of the results difficult and adjusted analyses not possible. However, the unadjusted baseline and lifetime analyses showed evidence (to varying degrees) that the following factors were associated with an increased odds of receiving a diagnosis of SAD compared with being a control: being single; having no close confidants; having a family history of mental illness, family history of psychosis, parental history of mental illness, parental history of psychosis. There were also differences between the analyses. The baseline analyses showed

evidence that the following were associated with an increased odds of receiving a lifetime diagnosis of SAD: living alone; having contact with family less than monthly; being unemployed; being male; being Black African; and never having had a long term relationship. The lifetime analyses showed evidence that the following were associated with an increased odds of receiving a lifetime diagnosis of SAD: being younger; and being African Caribbean. Due to small numbers in the SAD group, differences in findings between baseline and lifetime diagnoses are likely to be due to power issues (as the lifetime SAD group had even smaller numbers than the baseline SAD group). All that can be concluded is that psychosocial factors may be associated with SAD but as mentioned in section 8.2.3.1, this is not specific to SAD cases.

8.2.3.4. Differences by centre

There was evidence of an increased odds of being from London being associated with a diagnosis of schizophrenia and bipolar disorder in the baseline and lifetime diagnosis analyses. There was no such evidence for PMD and SAD groups. This difference could indicate that social context (described in chapter 3) is an important aetiological risk factor in schizophrenia and bipolar disorder, but not in PMD and SAD. Further research in this area could be informative as to the differences in aetiology between these disorders.

8.2.4. Comparisons with previous research

As discussed in chapter 3, there is very little previous research on the risk factors associated with PMD and SAD. Previous research has reported that PMD is more common in older people,[1, 27] in women,[77] and in Black African and African Caribbean ethnicities.[29] None of these findings have been supported by this thesis. In the case of age differences, this could be due to this thesis using age as a continuous variable and

other studies grouping age into a categorical variable. Differences in gender and ethnicity findings could be due to this thesis examining these variables compared with a non-psychotic control group rather than calculating these variables based on population based data. It is important to note that the findings on ethnicity from this thesis are from the same study that has shown differences in IRR for PMD,[81] the only difference being that odds ratios were used in this thesis.

The single study that investigated childhood adversity and PMD, and reported an association between PMD and specific types of childhood adversity[130] was based on the same dataset as this thesis, so the finding from this thesis of an association between PMD and any type of childhood adversity is not surprising.

The single study which examined PMD and life events and found an association between the two[156] was supported by the association between PMD, life events and life difficulties reported in this thesis.

8.2.5. Theoretical implications

Within the risk results chapter, a range of psychosocial risk factors were investigated for their association with PMD compared with other psychotic diagnoses. Kirkwood and Sterne note that "...examples where the results 'hit you straight between the eyes' are rare in medical research. This is because there is rarely such a one-to-one link between exposures and outcomes; there is usually a much more inherent variability from person to person."[444] This is supported by Schwartz & Susser who discuss the causes of disease as a "web of causation".[450] This is especially true in mental health. However, Schwartz & Susser have also highlighted that as risk factors work as a complex 'web' of interactions, by examining a single risk factor at a time, a full understanding of the

disease cannot be gained, and the "goal of causal explanation is to go beyond the identification of the causes of the disease to an understanding of the interplay among causes."[451] This suggests that an investigation of how these risk factors interact is needed. Within this study, it was not possible to look at interactions between key risk factors due to low power. However, this is a very important task for future research.

Within this thesis, differences between analyses based on baseline and lifetime diagnoses have been examined. The finding that there were differences in the identification of risk factors in the aetiology of PMD (specifically on childhood adversity) highlights the importance of taking diagnostic stability into account. Research on aetiology based on only a baseline diagnosis may well be inaccurate if we assume that lifetime diagnoses are more relevant as they are based on more information. However, as discussed above, knowing which diagnosis is 'right' is fraught with problems and as discussed in Chapter 2, the current diagnostic classifications systems have many problems which limits conclusions. Nevertheless, future research into aetiology in PMD and SAD should take diagnostic change into account as this leads to differing results. This links to the issue of whether diagnostic stability is a reflection of genuine diagnostic change or simply a lack of reliability. Either of these two could be true. However, whether this is diagnostic change or lack of reliability will not influence a clinicians' treatment, this will be dictated by the initial diagnosis and presenting clinical picture. Similarly, it will not change research diagnosis. As discussed in chapter 2, this will not be resolved until diagnostic classification become more accurate.

The DSM-5 offers no changes to the diagnosis of PMD. However, there are the following changes to the diagnosis of schizoaffective disorder: "Schizoaffective Disorder: The primary change to schizoaffective disorder is the requirement that a major

mood episode be present for a majority of the disorder's total duration after Criterion A has been met… It makes schizoaffective disorder a longitudinal instead of a cross-sectional diagnosis—more comparable to schizophrenia, bipolar disorder, and major depressive disorder, which are bridged by this condition."[452] It is stated that the change was made to improve the reliability, diagnostic stability, and validity of this disorder. It is yet to be seen if this change can improve the diagnostic stability of SAD and the influence of this change could have dramatically changed the results of this thesis if it had been published in time to be included here. Further research is needed to explore whether this change does improve reliability, diagnostic stability, and validity of this disorder.

8.2.6. Clinical implications

An association between a number of psychosocial risk factors and PMD and SAD has been established in this thesis. However, none of the risk factors identified in this thesis can be interpreted as having a causal effect due to the temporality issues surrounding prodromal periods, as discussed in section 8.2.2.5. If future research is able to indicate causality, this could indicate potential targets for prevention of disorder. In the meantime, the findings have indicated that cases who present with PMD are likely to be experiencing psychosocial inequality in the form of unemployment, social isolation (living alone, having no contact with friends or family, having no close confidants), life stress (life events and life difficulties) and possible psychological repercussions from childhood adversity. Thus, services are well placed to reduce this inequality.

Additionally, although causation cannot be concluded and the risk factors identified may not be easy to incorporate into public health interventions, this study adds to the

knowledge base of the disease, which may in turn, lead to preventative interventions or more effective treatments.[450]

8.3. Course and outcomes

8.3.1. Summary of results

8.3.1.1. Hypotheses

The following hypotheses were supported by either the baseline of lifetime diagnosis analyses or both:

1. PMD and SAD cases would have a lower prospective consistency compared with schizophrenia and bipolar disorder cases.
2. PMD cases would have a higher proportion of cases with an episodic course of illness and less with a continuous course of illness compared with schizophrenia cases.
3. PMD would have: longer remissions; shorter episodes; and will spend a smaller percentage of the follow-up psychotic, all compared with schizophrenia cases.
4. PMD cases would have a higher proportion of cases who attempt suicide over the follow-up compared with schizophrenia and bipolar cases.
5. SAD cases would have a higher rate of suicide attempts for those who do attempt, compared with schizophrenia and bipolar cases.
6. PMD cases would have a higher proportion of cases who self-harm over the follow-up compared with schizophrenia.
7. SAD cases would have a higher proportion of cases who self-harm over the follow-up compared with schizophrenia and bipolar cases.
8. PMD and SAD cases would have a higher rate of self-harm events for those who do self-harm, compared with bipolar cases.

9. In terms of social outcomes over follow-up, PMD cases would have a higher proportion of cases who are: employed; in a stable relationship; have close confidants; and a lower proportion of cases who have been to prison, all compared with schizophrenia cases.
10. In terms of social outcomes over follow-up, SAD cases would have a higher proportion of cases who are in a stable relationship compared with schizophrenia cases.
11. In terms of service use, PMD cases would have: a lower proportion of cases admitted; less hospitalisations; less days hospitalised; a lower percentage of the follow-up spent as an inpatient; a lower percentage of compulsory admissions; a lower proportion of cases being compulsorily admitted; and a lower percentage of hospitalisations involving the police, all compared with schizophrenia.
12. In terms of service use, SAD cases would have: less hospitalisations; a lower percentage of compulsory admissions; and a lower percentage of hospitalisations involving the police, all compared with schizophrenia.

The following hypotheses were not supported by this thesis:

1. PMD and SAD cases would have a higher retrospective consistency compared with schizophrenia and bipolar disorder cases (no difference with PMD cases, and SAD cases had lower retrospective consistency compared with schizophrenia and bipolar disorder).
2. SAD cases would have a higher proportion of cases with an episodic course of illness and less with a continuous course of illness compared with schizophrenia cases (no difference).
3. PMD would have more episodes compared with schizophrenia cases (PMD found to have fewer episodes).

4. SAD would have: longer remissions; more episodes; shorter episodes; and will spend a smaller percentage of the follow-up psychotic, all compared with schizophrenia cases (no difference on all variables).
5. PMD and SAD cases would have a higher proportion of cases who die (from all causes) over the follow-up compared with schizophrenia and bipolar cases (no difference).
6. PMD would have a higher rate of suicide attempts for those who do attempt, compared with schizophrenia and bipolar cases (no difference).
7. SAD cases would have a higher proportion of cases who attempt suicide over the follow-up compared with schizophrenia and bipolar cases (no difference).
8. PMD cases would have a higher proportion of cases who self-harm over the follow-up compared with bipolar cases (no difference).
9. PMD and SAD cases would have a higher rate of self-harm events for those who do self-harm, compared with schizophrenia cases (no difference).
10. In terms of social outcomes over follow-up, SAD cases would have a higher proportion of cases who are: employed (no difference); have close confidants (no difference); and a lower proportion of cases who have been to prison (no difference), all compared with schizophrenia cases.
11. In terms of service use, SAD cases would have: a lower proportion of cases admitted; fewer days hospitalised; a lower percentage of the follow-up spent as an inpatient; and a lower proportion of cases being compulsorily admitted, all compared with schizophrenia (no difference for all variables).

The hypothesis that PMD and SAD cases would have a higher proportion of cases who complete suicide over the follow-up compared with schizophrenia and bipolar cases could not be tested due to the small number of cases who completed suicide.

Before going on to interpret the outcome results, the methodological limitations of the study are examined.

8.3.2. Methodological considerations

Many of the methodological limitations considered in section 8.2.2 apply to the outcomes analyses and are discussed below.

8.3.2.1. Bias

8.3.2.1.1. Selection Bias

As mentioned in section 8.2.2.1.1, selection bias is defined as any error that arises in the process of identifying the study population.[424] In cohort studies, this is when the selection of an individual on the basis of their exposure or non-exposure is related to the outcome of interest. As previously discussed, most of the sample were help seeking individuals. This could relate to the service use outcomes, in that, cases who present to services for help may be more likely to represent to services in times of returning illness. This is turn could also relate to clinical outcomes as if a patient presents to services in times of returning illness, the illness is more likely to be treated and the episode will be shorter than those who do not re-present to services until the at crisis point which may only result in re-presenting due to other services intervening, e.g. police or A&E. However, selection bias in this form is unlikely to influence the outcome findings as in cohort studies exposure is ascertained before outcomes and therefore, selection bias is much less likely.[424]

However, the major source of bias in cohort studies is loss of participants over follow-up.[424] Differential loss to follow-up by exposure or outcome will lead to biased findings.

This is a problem within this thesis as the follow-up rate of all incidence cases was not 100%. This could have led to biases in the outcomes data. Those lost to follow-up could be lost to follow-up as they are well and have therefore lost contact with services and are therefore more difficult to trace. They could also be lost to follow-up as they are in prison or dead but we have failed to find this information. There were no differences in the follow-up rates between the different diagnoses and the overall follow-up rate was high (81.6%) but there is the possibility that the less ill PMD cases were more likely to be followed up and more ill schizophrenia cases being more likely to be followed up. As there was no measure of severity at baseline, it was impossible to assess.

8.3.2.1.2. Information Bias

As mentioned in section 8.2.2.1.2, interviewer bias can be a problem in epidemiological studies. Ascertainment of the exposure status is a problem in case control studies but not in cohort studies. However, ascertainment of outcome status in cohort studies is a problem as exposure status will be known and could lead to differential eliciting, recording or interpretation of outcomes.[424] Within this thesis, outcomes were gained through a combination of participant interview and clinical notes. Interviewers could have pressed cases with certain diagnoses more to illicit certain responses and similarly, clinical notes could have been interpreted differently between different diagnoses. It is likely that this kind of bias occurs subconsciously without the interview or notes reviewer even being aware of what is happening. This is a possible bias in this thesis as interviewers and note reviewers were not always blind to baseline diagnosis and is a limitation of the thesis.

As discussed in section 8.2.2.1.2, misclassification bias is a problem in case control studies, but it is also a problem in cohort studies. At the beginning of this study,

participants were classified as cases or controls and cases were further classified as having a number of different types of psychotic diagnoses. This classification at the beginning of the study was open to misclassification bias as well as the classification of the outcomes (e.g. continuous course of illness versus episodic course of illness; or suicide attempters versus non-attempter). The potential misclassification bias in diagnosis was addressed by re-diagnosing cases at follow-up based on the entire follow-up period information and a substantial difference in diagnosis was found between the two diagnoses. This is an improvement on many previous studies which did not account for misclassification bias in diagnosis. However, this study did not account for misclassification bias of case control status. Some controls could have become cases over the follow-up period but this was not measured. A potential improvement on similar future studies would be to follow-up controls as well as cases and use this information to address the case control misclassification bias.

8.3.2.1.3. Bias conclusions

As discussed in section 8.2.2.1.2, the role of bias in influencing an observed association must be considered in the interpretation of results. There is the possibility that interviewer bias was a problem within this thesis. However, it is not possible to know this for sure or to quantify the degree of bias. Therefore, the findings stand, but future research will be important to support, or in fact contradict these findings.

8.3.2.2. Chance

8.3.2.2.1. Interpretation of the p value and confidence interval

As discussed in section 8.2.2.2.1, examining both the p-value and the confidence interval of each finding rather than just the p value is incredibly important. As in the

case control study, the cohort study used a p-value of 0.1. Therefore, one in ten findings are likely to be due to chance and this must be borne in mind when interpreting the results.

8.3.2.2.2. Clinical versus statistical significance

As discussed in section 8.2.2.2.2, consideration of the clinical not just statistical significance is of vital importance. Within this thesis, there are findings which are statistically significant and clinically significant. For example, the finding based on lifetime diagnosis that PMD cases spend 5.2% of the follow-up in a psychotic episode compared with 76.7% of schizophrenia cases. This makes a massive difference to prognosis in PMD and schizophrenia cases. Similarly, the finding that based on lifetime diagnosis that 37% of PMD cases attempted suicide compared with 17% of schizophrenia cases has important implications for risk prevention. However, the finding that based on the baseline diagnosis the PMD group had a median number of one admission compared with two admissions in the schizophrenia group is unlikely to be of much clinical significance as the numbers are so similar.

8.3.2.2.3. Multiple testing

As discussed in section 8.2.2.2.3, increasing numbers of statistical tests increase the likelihood of finding a statistically significant difference due to chance. Within the outcomes results chapter, multiple tests were conducted but a p value threshold of 0.1 was used, it is likely that one in ten is a false positive finding. As with the risk factors analyses, this is a major limitation of the thesis.

8.3.2.2.4. Chance conclusions

Due to the multiple comparisons within the outcomes data (and the wide confidence intervals in some analyses, which indicate imprecise estimate of the effects), it is likely that some of the findings were due to chance. It was not possible to determine which findings but this must be borne in mind as a major limitation of the study when interpreting the results.

8.3.2.3. Confounding

As with the risk factors findings, it is possible that confounding influenced the results. Within the outcomes analyses there was no adjustment for key demographic variables (age, centre, gender and ethnicity). These factors could be confounding the results. There could also be confounding by variables which have not been measured. Specifically of relevance to this thesis is that this was a naturalistic study so a major potential confounder is treatment received over the follow-up. As it is unethical to withhold treatment this is an inevitable issue which must be borne in mind as a limitation.

8.3.2.4. Causality

It is unlikely that the baseline diagnosis analyses have any reverse causality involved as the diagnosis is determined before the outcomes are measured. However, it is possible that reverse causality is present in the lifetime diagnoses as these were determined at the same time as outcomes. This could also explain diagnostic change as outcomes could influence decisions made about diagnosis.

8.3.2.5. Study specific limitations

As discussed in section 8.2.2.5, issues surrounding diagnostic classifications are equally an issue within the outcome findings. Inaccurate diagnostic classification lead to inaccurate findings and current diagnostic classification is based on an imperfect descriptive system. This inevitably can only lead to imperfect findings but is an issue of psychiatry in general, not just a concern of this thesis.

As with Morgan et al.'s[448] issue surrounding the crude dichotomies used in research on risk factors, within the outcomes investigation, crude dichotomies have been used to simplify analyses. These include relationship status – 'single/divorced/separated' versus 'in a relationship'. These dichotomies are likely to over simplify the true nature of outcome for PMD cases. However, this thesis is the first long term (eight plus years) study based on an incidence sample and as such is a foundation for future research. Simplifications at this stage are likely to clarify what areas of research are focussed on in the future.

As with the risk factors examination, the outcomes investigation is based on new cases of the disorder under examination rather than a true incidence sample. This is not a problem for the outcomes findings however, as the findings inform clinicians as to prognosis for cases who present with a certain diagnosis at first contact with services.

Specific to the outcomes investigation, is an issue surrounding suicide attempts. Bromet et al.[160] state that an issue with all suicide studies is that not all suicides are recognized and recorded as such, meaning that any estimation of the prevalence of suicide is an underestimation. Within this thesis that is a distinct possibility. However, the main focus on outcomes in this thesis was to compare outcomes between the different

disorders. Therefore, although it is possible that the reporting of suicide attempts was underestimated, it is unlikely that this differed by diagnosis. This means that we can have confidence in these results.

As with the interpretation of the risk factors findings, Ioannidis's declaration that "most published research findings are false" is worth considering in the interpretation of the results .[443]

As with the risk factors chapter, the exclusion of cases aged over 65 years means the findings may not be valid for geriatric cases of PMD. Based on previous literature, 30% of PMD cases could have been missed due to age limits. The finding that many cases with a diagnosis of psychotic depression go on to receive a schizophrenia diagnosis may well be specific to a younger age group and warrants further research.

8.3.2.6. Methodological strengths

As in section 8.2.2.6, strengths of the outcomes section of the thesis include: accounting for diagnostic change; included incidence cases of all first episode cases presenting to services (not just inpatients or a prevalence sample); using a research diagnosis made by consensus; and consensus diagnosis blind to ethnicity. Additionally, diagnosis at follow-up was made blind to baseline diagnosis. Importantly, this thesis has improved on all previous research by combining these methodological strengths and thus can uniquely inform future research in the area.

8.3.3. Interpretation of the results

Despite the methodological limitations of this study, the results are very informative. Table 8-2 gives an overview of the outcomes findings.

Table 8-2: Overview of the outcome results

	PMD vs. SZ	PMD vs. BP	PMD vs. SAD	SAD vs. SZ	SAD vs. BP
Diagnostic stability					
Prospective consistency	PMD lower	PMD lower	=	SAD lower	SAD lower
Retrospective consistency	=	=	PMD higher	SAD lower	SAD lower
Course of illness outcomes					
Course of illness	PMD more episode and less continuous	PMD less episodic and more neither	= / PMD more episodic	=	SAD less episodic and more continuous and neither
Longest weeks of remission	PMD longer	=	= / PMD longer	=	SAD shorter
Number of episodes	PMD less	PMD less	= / PMD less	=	=
Longest episode in months (including first episode)	= / PMD shorter	PMD longer / =	=	=	SAD longer / =
Percentage of time psychotic during follow-up	PMD less	PMD more / =	= / PMD less	=	SAD more
Mortality and suicidality outcomes					
Death	=	=	=	=	=
Completed suicide	?	?	?	?	?
Suicide attempts	= / PMD more	= / PMD more	=	= / SAD more	= / SAD more
Self-harm	= / PMD more	PMD more	=	= / SAD more	= / SAD more
Social outcomes					
Employment status	PMD better	=	PMD better	=	SAD worse
Relationship status	PMD better	=	PMD better / =	= / SAD better	SAD worse / =
Close confidants	= / PMD better	=	=	=	=
Time in prison	PMD better / =	= / PMD worse	PMD better / PMD worse	SAD worse / =	SAD worse
Service use outcomes					
Binary hospitalisation	= / PMD less	PMD less	=	=	= / SAD less
Total number of hospitalisations	PMD less	PMD less	=	SAD less	=
Total number of days hospitalised	PMD less	=	=	=	=
Percentage of follow-up spent as an inpatient	PMD less	=	=	=	=
Percentage of admissions which were compulsory	PMD less / =	PMD less / =	=	SAD less / =	SAD less / =
Ever been compulsorily admitted	PMD less	PMD less	=	=	SAD less
Percentage of hospitalisations involving the police	PMD less	PMD less	=	SAD less	SAD less

= no difference in outcomes; ? comparison not possible; boxes with 2 entries indicates a difference between the baseline and lifetime analyses.

8.3.3.1. Diagnostic stability

The diagnostic stability analyses indicated that PMD and SAD had low diagnostic stability with the majority of cases moving to a diagnosis of schizophrenia. Predictors of diagnostic change in PMD cases were being younger at first contact; being younger at onset and being single. This has important clinical implications (see section 8.3.6).

8.3.3.2. Course of illness outcomes

In terms of course of illness, both baseline and lifetime analyses found PMD cases to be more episodic in their illness and less continuous, have longer remissions, less episodes and spend less time psychotic compared with schizophrenia. Additionally the lifetime analyses found PMD cases to have shorter episodes compared with schizophrenia cases. Both the baseline and lifetime analyses found PMD cases were less episodic and more 'neither episodic nor continuous' and have less episodes compared with bipolar disorder cases. Additionally the baseline analyses found PMD cases to have longer longest episodes and spent more time psychotic compared with bipolar disorder cases.
The lifetime diagnosis analyses also found that PMD was more episodic, had longer remissions, had fewer episodes and spent less time psychotic over the follow-up compared with SAD, but there were no differences between these groups according to the baseline analyses.

There were no significant differences between SAD and schizophrenia in either the baseline or lifetime analyses indicating a very similar course of illness in these cases. In comparison to bipolar cases in both baseline and lifetime analyses, SAD was found to be less episodic, more continuous and more 'neither episodic nor continuous' plus to have shorter remissions and to spend more time psychotic over follow-up. The baseline

analyses also found SAD cases to have a longer longest episode compared with bipolar cases.

Based on the above, there is evidence that SAD and schizophrenia have a very similar course of illness, but that the other disorders differ from each other with PMD having a better course than schizophrenia and SAD, but a worse course than bipolar, and SAD having a worse course than bipolar.

8.3.3.3. Mortality and suicidality outcomes

There were no differences in deaths over follow-up and attempted suicide could not be assessed due to the low numbers. However, while the baseline analyses showed very little differences between the groups in self-harm and none in suicide attempts, the lifetime results were very different. They revealed evidence that PMD cases attempted suicide more compared with schizophrenia and bipolar cases, and that of those who attempted suicide, SAD cases attempted more times compared with schizophrenia and bipolar cases. They also showed that more PMD cases self-harmed compared with schizophrenia cases and more SAD cases self-harmed compared with schizophrenia and bipolar cases, and of those who self-harmed, PMD and SAD cases self-harmed more compared with bipolar cases. Suicide attempt and self-harm outcomes has important clinical implications (see section 8.3.6).

8.3.3.4. Social outcomes

In terms of social outcomes, both the baseline and lifetime analyses revealed that PMD cases had better employment and relationship outcomes compared with schizophrenia cases. Additionally, the baseline analyses showed evidence that the PMD cases had better outcomes on time in prison, and the lifetime analyses showed evidence that PMD

cases had better outcomes in terms of close confidants. Compared with bipolar cases, there was only evidence of PMD cases having better social outcomes in the lifetime analysis of time in prison in which PMD had a worse outcome.

Compared with bipolar cases, SAD cases had worse outcomes according to both baseline and lifetime diagnoses on employment status and time in prison. Additionally, the baseline analyses supported SAD cases having worse relationship status outcomes. The analyses comparing SAD with PMD and schizophrenia were not very consistent in indicating that one group had better outcomes than the others.

These findings indicate that PMD cases have better social outcomes compared with schizophrenia cases, and SAD cases have worse social outcomes compared with bipolar cases. Other comparisons were not strongly indicative of a directional difference.

Marwaha and Johnson in their review of schizophrenia and employment state that low employment rates appear to reflect an interaction between social and economic pressures.[453] However, the findings of this thesis that statistically and clinically significantly higher numbers of PMD cases are employed compared with schizophrenia cases suggests that these issues might not be in play in PMD cases.

8.3.3.5. Service use outcomes

The results indicated that PMD cases had better service use outcomes compared with schizophrenia cases. Better service use outcomes are defined as less hospitalisations, days hospitalised, less time spent as an inpatient, compulsory admissions, and admissions involving the police. PMD cases also had better service use outcomes compared with bipolar cases on many of the variables. In light of the finding that PMD

cases are more likely to attempt suicide and self-harm, this finding is paradoxical. Logic would dictate that cases with a higher risk of suicide/self-harm are more in need of services. However, due to their better social outcomes, PMD cases may be more likely to have a social network which can be relied upon, which may reduce the need for inpatient care due to a reliance on informal care.

There were no differences between PMD and SAD cases in terms of service use outcomes, but there were several differences between SAD and schizophrenia and bipolar cases. SAD cases had less hospitalisations, less hospitalisations involving the police, and according to the baseline analyses, less compulsory admissions compared with schizophrenia cases. SAD cases were less likely to be hospitalised, were less likely to have been compulsorily admitted, had less hospitalisations involving the police, and according to the baseline analyses, had less compulsory admissions compared with bipolar cases.

These findings indicate that PMD and SAD cases have better service use outcomes compared with schizophrenia and bipolar cases. This has important clinical implications (see section 8.3.6).

8.3.3.6. Differences between baseline and lifetime analyses

There were some important differences between the baseline and lifetime analyses. For example, based on the lifetime diagnoses, PMD and SAD cases either had a higher proportion of cases who attempted suicide over the follow-up period or had a higher number of attempts for those who did attempt suicide compared with schizophrenia and bipolar cases. The baseline analyses supported no such difference.

As discussed in section 8.2.3.2, differences between the baseline and lifetime analyses could be due to power issues. However, in the outcomes analyses, over half the differences in findings involve lifetime diagnoses supporting a difference between groups where the baseline analyses found none. Therefore, power cannot be the issue in these instances. However, power could be the reason for instances where baseline diagnoses find a difference that is not supported by the lifetime diagnosis analyses. Instances where lifetime diagnoses support a difference between groups where the baseline analyses found none are likely to be due to diagnostic change.

As discussed in section 8.2.3.2, it is not possible to say which diagnosis is correct as both baseline and lifetime diagnoses both have their limitations. This is especially pertinent in regard to the outcomes analyses as diagnosis could change on the basis of outcome information, thus confounding the results. For example, the finding that PMD cases had better outcomes on a number of course of illness variables which were not identified by the baseline analyses could be due to the fact that those who have a worse outcome are more likely to be assumed to have schizophrenia. Also, diagnosis is partly about prognosis so a change in between baseline and lifetime diagnosis is expected as it is based on clinical picture across follow-up which will have included some information on outcome, which will have influenced the diagnosis. However, as discussed above, the result based on each diagnosis is simply different, and until a more reliable diagnostic system is in place, our conclusions are limited.

8.3.3.7. Differences between PMD and SAD

There were some areas where there were no differences in outcomes between PMD and SAD cases, such as service use, mortality and suicidality, and prospective consistency. However, although as discussed in Chapter 2 there are some striking similarities in

diagnostic overlap between PMD and SAD, there were still some important differences. For example, based on lifetime diagnoses, PMD cases seem to have a better course of illness compared with SAD cases. However, based on the baseline diagnoses there were no differences in course of illness indicating that perhaps these disorders are so similar that differences in the course of the illness can determine them apart, but perhaps this is a superficial difference as there is no real evidence of differences in mortality and suicidality, social outcomes or service use.

8.3.4. Comparisons with previous research

As discussed in chapter 4, there is a fair amount of previous research on the course of illness and outcomes in cases with PMD but less so with SAD cases. The hypotheses of this thesis were created in line with previous research but only around half of the hypotheses were supported by the findings of this thesis. This is likely due to methodological differences between this thesis and previous research as this thesis was the first study to conduct a long-term follow-up of incidence cases and the first to account for diagnostic change.

The consistent finding from previous literature that PMD cases are less characterised by a continuous course type and more by an episodic course type[200, 229, 258] was supported by both the baseline and lifetime analyses, as was the consistent finding from previous literature that PMD cases have better employment outcomes compared with schizophrenia cases.[180, 227, 258, 259, 262] However, the consistent finding that SAD cases have better employment outcome compared with schizophrenia cases[239, 258, 259, 262] was not supported by either the baseline or lifetime analyses in this thesis. This could be due to power issues.

The finding from previous literature that more PMD cases self-harm compared with schizophrenia cases[1] was supported by the lifetime analyses but not baseline analyses.

8.3.5. Theoretical implications

As with the risk factors analysis, the baseline and lifetime diagnosis analyses gave slightly differing results, some of which were clinically very important (attempted suicide and self-harm being higher in PMD and SAD cases). This difference is important to note and future research examining course and outcomes of illness should take diagnostic change into account as this can dramatically alter results.

The finding that PMD cases had better social, course of illness and service use outcomes but were more likely to attempt suicide or self-harm seems incongruous. The clinical implications of this are discussed in section 8.3.6. However, there are also theoretical implications surrounding this in relation to the mechanism of this. For example, could it be that cases who have better outcomes in some areas are seen to be less in need of the support of mental health services and thus receive less support, leaving them vulnerable to suicidal or self-harming behaviour? Alternatively, could it be that PMD cases have less continuous difficulties but their episodes are more severe when they do occur, and this severity is characterised by suicidal and self-harming behaviour? Or could it be that due to their better social functioning, they are able to hide their illness until it becomes a crisis and suicidal and self-harming behaviour ensues? Further research into this could be very useful in informing harm reduction strategies and risk assessment in these cases.

8.3.6. Clinical implications

There are a number of clinical implications which come out of the outcomes analyses. The first regards diagnostic stability. As diagnostic stability was low for PMD and SAD cases, and as the majority of changes moved to a diagnosis of schizophrenia, clinicians should look out for change in diagnosis in these groups as it has important implications in terms of treatment (i.e. a change in medication regime).

Secondly, linked to diagnostic stability is the finding that a sizeable proportion of PMD cases become schizophrenia over time. In light of this, the decision by many early intervention services to exclude depressive psychosis cases from their remit should be re-evaluated. Excluding cases based on an initial diagnosis of PMD could lead to patients with schizophrenia (and other psychotic disorders) missing out on the benefit of early intervention services.

Thirdly, the results indicate that clinicians should be concerned with suicide attempts in PMD cases as it was more likely to have occurred in these patients compared with schizophrenia and bipolar disorder cases. PMD and SAD cases were also more likely to self-harm compared with schizophrenia cases which is another important issue for clinicians to be aware of.

Fourthly, PMD cases had better social and course of illness outcomes and had more positive service use outcomes. In light of these incongruous findings between suicide/self-harm outcomes and social/service use outcomes, clinicians should be aware of issues surrounding self-harm and suicide attempts even in cases who seem to be having a favourable outcome following first episode. Additionally, although clinicians may be cautiously optimistic about outcomes in PMD cases based on some of the social outcome results in this thesis regardless of the incongruous findings on suicide/self-

harm, the finding that may cases switch to a diagnosis of schizophrenia may be reason for clinicians not to be overly optimistic with their PMD patients and their families. This raises the dilemma of the usefulness of giving a specific diagnosis during a first episode of psychosis and perhaps giving a diagnosis of psychosis and waiting until the clinical picture is clearer would be useful in terms of managing expectations.

8.4. Future research

As discussed above, there are various areas of research that spawn from this thesis. Firstly, due to the low numbers and therefore, difficulty in interpreting the results around the SAD group, further research is needed to understand the risk factors and long term outcomes in this group. Secondly, although a number of risk factors have been examined, examining the interaction of these factors was not possible due to power issues and a bigger sample is required to examine interactions. A bigger sample would also allow an investigation of specific types of life events and difficulties which were not examined within this thesis. Thirdly, as this is the first study to examine risk factors and long term outcomes in PMD cases, an attempt to replicate the results with a different sample could strengthen the findings and conclusions. In relation to this replication, Warner[93] described the following outcome areas as vitally important in patients with psychosis: unemployment; poverty; homelessness; time in prison and social isolation. Within this thesis, poverty and homelessness has not been addressed, only unemployment, time in prison and social isolation. Thus future research should include poverty and homelessness. Fourthly, differences in risk between the centres of London and Nottingham could not be examined in more detail due to the limitations of the study. However, there are clear differences in the risk of PMD and SAD between the London and Nottingham sites. This could have been due to differential diagnostic classification between the sites which is a potential source of bias. However, it could

also be due to differences between the sites: urbanicity; population density; ethnic density; or deprivation levels (as described in section 5.4). It could also be due to a number of unknown factors. Future research could examine these factors in more depth to determine what neighbourhood level factors influence the aetiology of PMD and SAD. Finally, Morgan points out that there is a need to move on from the simple analyses of demographics to a "detailed consideration of the social phenomena that may underlie these broad associations".[62] Morgan states that this also need to occur for other area such as trauma – the association between mental illness and trauma is no longer enough, we need to examine the mechanisms of these phenomenon.[62]

8.5. Conclusions

The findings of this thesis suggest that accounting for diagnostic change when examining risk factors and course of illness in PMD and SAD cases is of particular importance. Analyses indicate that social risk factors play a part in the aetiology of PMD but no more so than in schizophrenia and bipolar cases. PMD cases appear to have better social and services use outcomes but are more at risk of self-harming or attempting suicide. Due to low numbers in the SAD group, the conclusions based on this group are very limited.

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APPENDICES

Appendix A Data extraction form

Paper reference number	
Study ID	
Author	
Year	
Title	
Place	
Setting / selection process / Who	
Comparison groups	
Number of Ps in each group	
Study design	
Diagnostic Tool	
Length of follow-up	
follow-up rate in each group or overall	
follow-up measures	
Findings PMD group	
Findings comparison group	
Prospective / Retrospective / Historical	
Compares Congruence?	
Notes	

Appendix B Newcastle – Ottawa Quality Assessment Scale

COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection, Outcome and Analyses categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort

a) truly representative of the average _____ (describe) in the community*
(All potential patients or a random sample of potential patients or consecutive patients)

b) somewhat representative of the average _____ in the community*
(80+% of the potential population and there is a full description of refusals)

c) selected group of users e.g. nurses, volunteers
(80+% of the potential population and no description of refusals or <80% of the potential population)

d) no description of the derivation of the cohort
(no description)

2) Selection of the non exposed cohort

a) drawn from the same community as the exposed cohort*

b) drawn from a different source

c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

a) secure record (e.g. surgical records)*

b) structured interview*

c) written self report

d) no description

Comparability

4) Comparability of cohorts on the basis of the design or analysis

a) study controls for _____ (select the most important factor)*

b) study controls for any additional factor*

c) study conducted multivariate analyses to control for confounders**

Outcome

5) Assessment of outcome

a) independent blind assessment*

b) record linkage*

c) self report

d) no description

6) Was follow-up long enough for outcomes to occur *(at least 1 year)*

a) yes (select an adequate follow-up period for outcome of interest)*

b) no

7) Adequacy of follow-up of cohorts

a) complete follow-up - all subjects accounted for*
(100% follow-up)

b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow-up, or description provided of those lost)*
(80% or over, or examined differences between followed-up and non-followed-up groups (with comparison))

c) follow-up rate < ____% (select an adequate %) and no description of those lost
(Under 80% and/or no examining of differences between followed-up and non-followed-up groups)

d) no statement
(No description)

Analyses

8) Have appropriate analyses been conducted? (continuous data analysed as a continuous variable and not transformed into categorical data and see 'how to read a paper')

a) Yes*

b) No

9) Have confidence intervals been reported?

a) Yes*

b) No

10

* 1 point
** 2 points

Appendix C Screening Schedule for Psychosis

Screening Schedule for Psychosis

There should be at least one "yes" in Section A or two in Section B

A Has the patient ever presented any of the following:
(i) Hallucinations or pseudo-hallucinations in any modality
(ii) Delusions
(iii) Marked thought and speech disorder (e.g. incoherence, irrelevance, thought blocking, neologisms, incomprehensibility of speech) other than simple retardation or acceleration
(iv) Marked psychomotor disorder (e.g. negativism, mutism or stupor, catatonic excitement, constrained attitudes or unnatural postures maintained for long periods) other than simple retardation or acceleration
(v) Emergence or marked exacerbation of bizarre and grossly inappropriate behaviour (e.g. talking or giggling to self, acts incomprehensible to others, loss of social constraints, etc)

B A definite change of personality and behaviour manifested in any of the following:
(i) Marked reduction or loss of interests, initiate and drive, leading to serious deterioration of the performance of usual activities and tasks
(ii) Emergence or marked exacerbation of social withdrawal (active avoidance of communication with other people)
(iii) Severe excitement, purposeless destructiveness or agression
(iv) Episodic or persistent states of overwhelming fear or severe anxiety
(v) Gross and persistent self-neglect

Appendix D Patient Information Sheet

ÆSOP

UNDERSTANDING THE CAUSES OF MENTAL HEALTH PROBLEMS
Please read this carefully if you wish to participate in our study.
Your participation is entirely voluntary.

General information Sheet for Patients

We are carrying out a study at the Maudsley/ Bethlem and South Western Hospital on new patients to try to find out which factors lead to the development of mental health problems in different sections of the population. As illness can be caused by physical problems or by stress in people's lives, we would like to find out how you are feeling at the moment as well as how you were before you came into the hospital, to see if any of your experiences played a part in why you became ill.

We would like to come and speak to you on a few occasions while you are in hospital to find out how you are, and ask you about any difficulties or problems that you may be having.

We would like to perform an MRI scan of your brain in the radiology department, which takes less than an hour. This is a new type of scan which gives a clearer picture of the brain and does not involve X-rays. You will be accompanied by a member of staff during this who can answer any questions you might want to ask. Later on, we would like to arrange for you to do some concentration and memory tests, which take about two hours.

We would also like to have a chat with your closest relative, preferably your mother, or someone else who is close to you and who would know about recent events in your life.

Finally, we would like to meet you again in a year's time to ask how you are getting on.

Anything you say will be treated in the strictest confidence.

If you decide not to be a part of the study, this will not affect in any way the care you receive at the hospital. If you do decide to take part you are free to withdraw from the study at any time without having to say why. We hope you will agree to take part in this study so that your help may contribute to improving the care offered by hospitals.

If you would like to ask any questions or want to find out about anything else at all, please telephone the research team on 0171 919 3492, and any of the researchers will be happy to speak to you. Alternatively, please telephone Kevin Morgan on 0171 740 5186.

The project is based at:
The Social Psychiatry Section
MRC Research Centre
Institute of Psychiatry
De Crespigny Park
London SE5 8AF

Appendix E Patient general consent form

ÆSOP

UNDERSTANDING THE CAUSES OF MENTAL HEALTH PROBLEMS

Researchers: Professor J. Leff, Professor R. Murray

PATIENT CONSENT FORM

Brief information about the study

We are studying the factors that lead to the development of mental health problems in different sections of the population. As part of this study we are interviewing people like yourself who have made contact with the psychiatric services for the first time. We would like to interview you to ask about things that might have happened to you in the past or difficulties you may have had recently that could explain why you have become ill. The information you give us is strictly confidential and your name will not be used in any records we keep.

It would also be very helpful if we could interview some of your relatives to find out whether anyone else in your family has had a similar illness.

Consent section

I agree to being interviewed for this study. I understand that I can withdraw from the interview at any stage and that it will not affect the treatment I am given.

Signed ……

I agree to my relatives being contacted for a possible interview

Signed ……

Witness ……..

Appendix F Control general consent form

ÆSOP

UNDERSTANDING THE CAUSES OF MENTAL HEALTH PROBLEMS

Researchers: Professor J. Leff, Professor R. Murray

COMMUNITY CONSENT FORM

Brief information about the study

We are studying the factors that lead to the development of mental health problems in different sections of the population. We are interviewing people in the community who are in good health, as well as patients, in order to compare their experiences.

We would like to interview you to ask about things that may have happened to you in the past or difficulties that you may have had. The information you give us is strictly confidential and your name will not be used in any records we keep. It would also be very helpful if we could interview one of your parents to find out about your early childhood. This interview would be very short and could be conducted by telephone.

Consent section

I agree to being interviewed for this study. I understand that I can withdraw from the interview at any stage.

Signed ……..

I agree to my relative being contacted for a possible interview.

Signed ……..

Witness ……..

Appendix G Psychosis Screening Questionnaire

ÆSOP

PSYCHOSIS SCREENING QUESTIONNAIRE (PSQ)

Interviewer …….. Date……

ÆSOP ID ☐☐☐☐☐

Code: No = 0 Unsure = 1 Yes = 2

In this health survey we have to ask about a whole range of experiences. Some of these experiences are quite rare. However, I would be very much obliged if you would bear with us and answer the questions I am going to ask you now.

Q1. Over the past year, have there been times when you felt very happy indeed without a break for days on end? ☐

(a) Was there an obvious reason for this? ☐

(b) Did your relatives or friends think it was strange or complain about it? ☐ **If 2 stop**

Q2. Over the past year, have you ever felt that your thoughts were directly interfered with or controlled by some outside force or person? ☐

(a) Did this come about in a way that many people would find hard to believe, for instance through telepathy? ☐ **If 2 stop**

Q3. Over the past year, have there been times when you felt that people were against you? ☐

(a) Have there been times when you felt that people were deliberately acting to harm you or your interests? ☐

(b) Have there been times when you felt that a group of people was plotting to cause you serious harm or injury? ☐ **If 2 stop**

Q4. Over the past year have there been times when you felt that ☐

something strange was going on?

(a) Did you feel it was so strange that people would find it very hard to believe? ☐ **If 2 stop**

Q5. Over the past year, have there been times when you heard or saw things that other people couldn't ☐ **If 1 or 2 stop**

(a) Did you at any time hear voices saying quite a few words or sentences when there was no-one around that might account for it? ☐ **If 2 stop**

Q6. Have you ever received treatment for any psychiatric or psychological problem?

……

……..

Appendix H Medical Research Council Socio-demographic Schedule

SOCIO- DEMOGRAPHIC SCALE

Note: For coding missing values in each field: -77= Don't know; -88= Refused to answer; -99= Not applicable

Starting Time: _____ **Finishing Time:** _____

Date of interview: **Centre No:**

Interviewer ID No. **Resp. ID No:**

1) Sex:

1. Male *2.Female* | |

2) Date of Birth: | | | | | | |

3) Age: _____ | |

1. 16-25 *2. 26-35*
3. 36-45 *4. 46-55*
5. 56-65

4) Religion: | |

1.	*Catholic*	*2.*	*Church of England*
3.	*Methodist*	*4.*	*Muslim*
5.	*Hindu*	*6.*	*Sikh*
7.	*Pentecostal*	*8.*	*Rastafarian*
9.	*Baptist*	*10.*	*Presbyterian*
11.	*Church of Ireland*	*12.*	*Jewish*
13.	*Other (please specify)*		_____
14.	*None*		

RESIDENTIAL

5) Where were you born? **If UK go to Q10 on page 7**

Explicit town if UK…….. and hospital……
and country if abroad …… and hospital ……

1. *UK*
2. *Ireland*
3. *Europe*
4. *Indian sub-continent (India, Pakistan, Bangladesh)*
5. *Caribbean*
6. *Africa*
7. *Asian Other (China, Vietnam, etc)*
8. *Other (please specify……)*

6) How old were you when you moved to the UK?

Note: For Questions 7-10, please probe for as much information as possible on all people that the respondent resided/s with, and rate each one.

7) Who did you live with before moving here? 1= Yes 0= No

7.1 Mother ☐

7.2 Father ☐

7.3 Parents ☐

7.4 Sibling (s) ☐

7.5 Spouse/ Partner ☐

7.6 Children ☐

7.7 Grandparent(s) ☐

7.8 Aunt(s)/ Uncle(s) ☐

7.9 Cousins ☐

7.10 Other relative(s) ☐

7.11 Step Mother ☐

7.12 Step Father ☐

7.13 Step- children ☐

7.14 Step-siblings ☐

7.15 Adoptive Parents ☐

7.16 Adoptive sibling(s) ☐

7.17 Half sibling(s) ☐

7.18 Family friend(s) ☐

7.19 Own friend(s) ☐

7.20 Alone ☐

7.21 Other ……. ☐

8) Who did you come with? 1= Yes 0= No

7.1 Mother ☐

7.2 Father ☐

7.3 Parents ☐

7.4 Sibling (s) ☐

7.5 Spouse/ Partner ☐

7.6 Children ☐

7.7 Grandparent(s) ☐

7.8 Aunt(s)/ Uncle(s) ☐

7.9 Cousins ☐

7.10 Other relative(s) ☐

7.11 Step Mother ☐

7.12 Step Father ☐

7.13 Step- children ☐

7.14 Step-siblings ☐

7.15 Adoptive Parents ☐

7.16 Adoptive sibling(s) ☐

7.17 Half sibling(s) ☐

7.18 Family friend(s) ☐

7.19 Own friend(s) ☐

7.20 Alone ☐

7.21 Other ……. ☐

9) When you came to the UK, with whom did you live? 1= Yes 0= No

7.1 Mother ☐

7.2 Father ☐

7.3 Parents ☐

7.4 Sibling (s) ☐

7.5 Spouse/ Partner ☐

7.6 Children ☐

7.7 Grandparent(s) ☐

7.8 Aunt(s)/ Uncle(s) ☐

7.9 Cousins ☐

7.10 Other relative(s) ☐

7.11 Step Mother ☐

7.12 Step Father ☐

7.13 Step- children ☐

7.14 Step-siblings ☐

7.15 Adoptive Parents ☐

7.16 Adoptive sibling(s) ☐

7.17 Half sibling(s) ☐

7.18 Family friend(s) ☐

7.19 Own friend(s) ☐

7.20 Alone ☐

7.21 Other ……. ☐

10) With whom do you live now? 1= Yes 0= No

7.1 Mother ☐

7.2 Father ☐

7.3 Parents ☐

7.4 Sibling (s) ☐

7.5 Spouse/ Partner ☐

7.6 Children ☐

7.7 Grandparent(s) ☐

7.8 Aunt(s)/ Uncle(s) ☐

7.9 Cousins ☐

7.10 Other relative(s) ☐

7.11 Step Mother ☐

7.12 Step Father ☐

7.13 Step- children ☐

7.14 Step-siblings ☐

7.15 Adoptive Parents ☐

7.16 Adoptive sibling(s) ☐

7.17 Half sibling(s) ☐

7.18 Family friend(s) ☐

7.19 Own friend(s) ☐

7.20 Alone ☐

7.21 Other ……. ☐

11) Indicate total number in house hold ……

12) (**Do not ask this question**) Rate type of household from Q.10

1. Single person
2. Couple
3. Couple + children
4. Single parent and children
5. Grandparents/ couple + children
6. Grandparents/ single parent + children
7. Siblings + children
8. Friend
9. Other (Specify) ……

13) Who is the head of your household? ……
(ie. main income earner/spiritual head/main decision maker)
[If single person only, go to Q.15]

0. Self (Patient/ control)
1. Spouse/ co-habitee
2. Parent
3. Son/ daughter
4. Sibling
5. Other relative (specify) ……..
6. Friend
7. Co-resident
8. Other (specify) ……..

14) What is your position in the household? ……
[for those in non-single person households go to Q.17]

1. Spouse/ co-habitee
2. Parent
3. Son/ daughter
4. Sibling
5. Other relative (specify) ……..
6. Friend
7. Co-resident

15) When was the last time that you lived with others? ……..

0. Within the last year
1. Within last 1-2 years
2. Within last 2-3 years
3. More than 3 years ago

16) Is there any reason why you live alone?

(reason) …….

0. No reason
1. Positive decision
2. Of necessity

17) Where did you live during the first 16 years of your life, starting with place born, all different towns since and the number of years you lived there?

Country/ Town	*Area*	*No. of years*
……	……	……..
……	……	……..
……	……	……..
……	……	……..
……	……	……..
……	……	……..

18) How old were you when you left your parental/ care giving home? ……..

19) When did you move to this town/ area? dd/mm/yy ……./……../……

1. Less than 6 months ago *2. 6-12 months ago*
3. 1-2 years ago *4. 2-4 years ago*
5. 5 years ago and over

20) How many addresses have you lived at in the last 3 years?

(1,2, 3 etc) ……

21) When did you move to this address? dd/mm/yy ……/……./……..

1. Less than 6 months ago *2. 6-12 months ago*
3. 1-2 years ago *4. 2-4 years ago*
5. 5 years ago and over

22) **Interviewers- Rate type of current accommodation:**

1. Detached house
2. Semi- detached house
3. Terraced house
4. Flat\ Maisonette in house
5. Purpose built flat
6. Multi- storey block/flat
7. Bedsitter
8. Hostel
9. Squat
10. Other (specify) **…….**

23) Do you own the house/ flat or is it rented accommodation?

1. *Yes: Self/Joint owner occupied*
2. *No: Family owner occupied*
3. *No: Private rented*
4. *No: Local authority rented*
5. *No: Housing association rented*
6. *Other (specify)*

24) How many rooms do you have in you accommodation? (1, 2, 3, etc.)
(Excluding kitchen and bathroom)

RELATIONSHIP/ FAMILY

25) What is your current relationship status? ☐

1. *Married/ Living with someone*
2. *Single in steady relationship*
3. *Single in casual relationship(s)*
4. *Single- no partner*
5. *Divorced*
6. *Widowed*
7. *Separated*

26) Have you ever:

26a) been divorced? ☐
(0= never, 1= once, 2= twice, etc)

26b) been separated? ☐
(0= never, 1= once, 2= twice, etc)

26c) been widowed? ☐
(0= never, 1= once, 2= twice, etc)

26d) lived with a long-term partner (over 2 years)? ☐
(0= never, 1= once, 2= twice, etc)

27) How many children do you have? ☐☐
(0= none, 1= one, etc)

28) Have you ever lost a child? **[Probe for miscarriage/ death]** ☐
(0= none, 1= one, etc)

If applicable 28a) How old was the child? …… ☐☐

28b) How old were you?..... ☐☐

28c) What happened? .....

…….

29) Is your mother alive? **[If no go to 31]** ☐
0= No *1=Yes* *2=Don't know*

30) How old is your mother now? ..... ☐☐

31) How old were you when she died? ☐☐

32) Where was your mother born? **[If UK. Go to 34]**

Explicit town if UK ..... and country if abroad.....

1. *UK*
2. *Ireland*
3. *Europe*
4. *Indian sub-continent (India, Pakistan, Bangladesh)*
5. *Caribbean*
6. *Africa*
7. *Asian Other (China, Vietnam, etc)*
8. *Other (please specify.....)*

33) How old was your mother when she came to UK?.....

34) Is your father alive? **[If no go to 36]**

0=No *1=Yes* *2= Don't know*

35) How old is your father now?.....

36) How old were you when he died?

37) Where was your father born? **[If UK. go to 39]**

Explicit town if UK..... and country if abroad.....

1. *UK*
2. *Ireland*
3. *Europe*
4. *Indian sub-continent (India, Pakistan, Bangladesh)*
5. *Caribbean*
6. *Africa*
7. *Asian Other (China, Vietnam, etc)*
8. *Other (please specify.....)*

38) How old was he when he came to the UK?.....

39) Were you ever separated from your mother before aged 17?.... **[If no go to 42]**

0= No *1=Yes*

40) How old were you? .....

41) How long was it for? .....

1. less than 1 year *2. 1-2 years*
3. 2-4 years *4. 4+ years*

42) Were you ever separated from your father before aged 17? **[If no go to 45]**
0= No *1=Yes*

43) How old were you? .....

44) How long was it for? .....
1. less than 1 year *2. 1-2 years*
3. 2-4 years *4. 4+ years*

45) [**If separated from either or both parents**, press reason for the separation: eg. migration, parent separation, illness, prison etc and write down verbatim**. If not separated from either go to Q. 47**]

.....

.....

46) Who looked after you during this time? .....
1. Grandparent/s
2. Aunts/ Uncle/s
3. Sibling/s
4. Step- parent/s
5. Other relatives (specify).....
6. Adoptive parent/s
7. Family friend/s
8. Foster parents/ Social services care
9. Other (specify) .....

47) Who was your main care giver for most of your childhood? .....
0. Natural parent/s
1. Grandparent/s
2. Aunts/ Uncle/s
3. Sibling/s
4. Step- parent/s
5. Other relatives (specify) .....
6. Adoptive parent/s
7. Family friend/s
8. Foster parents/ Social services care
9. Other (specify) .....

47a) If the answer is natural, step or adoptive parent/s, please specify if the main caregiver was:
1. Mother
2. Father
3. Both

48) How many brothers and sisters do you have?

(Draw a genealogy on reverse of sheet detailing gender, ages and date of births of siblings. Ensure that it includes information on full and half siblings, and also on shared parents, if applicable)

48a) Brothers (0,1,2,3.....).....

48b) Sisters (0,1,2,3.....).....

48c) Total (0,1,2,3.....).....

49) Have you any who have died?

48a) Brothers (0,1,2,3.....).....

48b) Sisters (0,1,2,3.....).....

48c) Total (0,1,2,3.....).....

If applicable, who has died, when and how?

.....

.....

50) What is/ was your position in the family? .....

1. Eldest
2. Middle
3. Youngest
4. Twin
5. Only Child

51) Do you share the same two parents with all your siblings?

0= No *1= Yes*

EDUCATION

52) Where did you go to secondary school? (name and address of school)
.....

1. UK
2. Ireland
3. Europe
4. Indian sub- continent (India, Pakistan, Bangladesh)
5. Caribbean
6. Africa
7. Asian Other (China, Vietnam, etc)
8. Other
9. More than one country (specify) .....

53) What was the highest level of education you reached?
Write qualifications attained below and where attained
1. No qualifications
2. GCSE/ CSE
3. O' levels
4. A' levels
5. Vocational/ college (B.Tecs/NVQs etc)
6. Teaching/HND/ nursing
7. University/ Professional qualifications

.....
.....
.....

54) Have you ever needed remedial education **[If 'no' go to Q.57]**

1. Yes
2. No

55) What special help did you receive? .....

1. Reading and/ or writing
2. Maths
3. Both 1 and 2
4. Other (specify) .....

Write verbatim the type of education received

56) At what age did you receive this help? .....

57) Have you ever been studying during the past year?.....

[If no go to 60]

0. No
1. Yes, full-time student
2. Yes, part-time student
3. Yes, part-time student and part-time working
4. Yes, part-time student and full-time working
5. Yes, full-time student and full- time working
6. Yes, have been a student for some time but have discontinued

If yes and if appropriate, write down the qualifications attained below and where attained

.....
.....

58) What kind of education were you receiving? .....

0. General (eg. reading, writing and arithmetic)
1. Specialised- training for a trade or apprenticeship (specify).....
2. Specialised- academic (specify nature of course) .....

59) How have you done in your studies in the last year? .....

0. Excellent
1. Good
2. Fair
3. Poor

60) Since you left ..... have you had any further skills training/formal education? Or [Apart from this last year] have you had any other type of formal education?

0. Yes
1. No

61) If yes, what kind and how long attended?

Type:	*Months:*	*Years:*
.....	.....	.....
.....	.....	.....
.....	.....	.....

EMPLOYMENT

62) Are you currently employed? **[if no go to Q.77]**

1. Yes
0. No

63) In total, how many years have you been employed?

1. Less than 1 year
2. >1-<3
3. >3-<5
4.>4-<10
5.>10
9. Not known

64) Have you changed jobs in the last 12 months? .....

0. No change
1. One change
2. Two changes
3. Three or more changes

65) If applicable, in what way has it changed? (promotions, demotions etc.) .....

0. Same status
1. Lower status
2. Higher status

66) Please give your current job title? .....

[please rate in one of the following categories]

1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces

67) In your current occupation, are you working:

1. At home in sub-contracted work
2. Self employed
3. In a family business
4. For others
5. Other (specify) .....

68) Are you working full-time or part-time? .....

0. Full- time only, normal conditions
1. Full- time only, sheltered conditions
2. Part-time only, normal conditions
3. Part- time only, sheltered conditions
4. Some full-time and some part-time periods, normal conditions
5. Some full-time and some part-time periods, sheltered conditions
6. Other (specify)

69) What is your annual salary like for that job?

0. <6000
1. 6,000- 8,500
2. 8,500- 12,000
3. 12,000- 15,000
4. 15,000- 20,000
5. 20,000- 25,000
6. 25,000+

70) What was/ is the degree of responsibility in your job?.....

0. Little: works under constant supervision
1. Moderate: works mainly on his/own with occ.supervision
2. High: person supervises others
3. Nature of work doesn't involve supervision by others

71) How have you been doing in your job in the last year? .....

0. Attends work regularly, performance adequate for job
1. Attends work regularly, performance good
2. Absent from work occasionally, decline in work standard or person feels they are struggling to cope
3. Absent from work frequently, has been fired because of poor Performance or gross neglect at work

72) Is this the kind of work you have been doing for the most of your life?

1. Yes
2. No

73) If no, then what has been your main occupation? (title).....

[please rate in one of the following categories]

1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces

74) Do you have another job in addition to your regular job outside the home?
(title) ..... **[If no go to 76]**

0. No other job
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces

75) What is your annual salary for this job?

0. <6000
1. 6,000- 8,500
2. 8,500- 12,000
3. 12,000- 15,000
4. 15,000- 20,000
5. 20,000- 25,000
6. 25,000+

76) In the last 2 years have you ever worked in another job in addition to your regular job? (title) .....

0. No other job **[If no go to Q. 86]** ☐

1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces

77) Did you ever work in the last 12 months? ..... **[If more than 0 go to Q.80]** ☐
(Rate employment in the past 1 year)

0. No work
1. Has had 1 or more months of unemployment
2. Working practically all the time

78) Why haven't you worked? ..... ☐

0. House-person
1. Student
222
2. Physical Disability
3. Mental Illness
4. Unable to find job
5. Retired
6. Other (specify).....

79) Have you ever had a paid job? **[If no go to Q.85]** ☐

1. Yes
0. No

80) What was the last occupation you had? (title)..... ☐

0. No other job
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces

81) How many years ago was that? (1,2,3 etc.)..... ☐☐

82) Was it full-time or part-time?..... ☐

0. Full- time only, normal conditions
1. Full- time only, sheltered conditions
2. Part-time only, normal conditions
3. Part- time only, sheltered conditions
4. Some full-time and some part-time periods, normal conditions
5. Some full-time and some part-time periods, sheltered conditions
6. Other (specify)

83) At that time were you working:

1. At home
2. For yourself
3. In a family business
4. For others

84) What were your earnings like?.....

0. <6000
1. 6,000- 8,500
2. 8,500- 12,000
3. 12,000- 15,000
4. 15,000- 20,000
5. 20,000- 25,000
6. 25,000+

85) As you are not working are you able to claim benefits? If so, which ones?

1. Yes *2. No*

1. Housing

2. Family

3. Income

4. Disability

5. Other

86) Apart from formal paid work, have you done any type of voluntary work in the past two years/ including odd jobs helping friends?

1. Yes
0. No

I WOULD NOW LIKE TO ASK YOU SOME QUESTIONS ABOUT YOUR FAMILY'S OCCUPATIONS.

87) *If applicable* what type of work does your partner do? (title) .....

0. Unemployed
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces
8. Student
9. Retired
10. House-person

88) What was/is your father's main occupation? (title).....

0. Unemployed
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces
8. Student
9. Retired

89) What was your father's occupation when you were born? (title) .....

0. Unemployed
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces
8. Student
9. Retired

90) What was/is your mother's main occupation? (title).....

0. Unemployed
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces
8. Student
9. Retired

91) What was your Mother's occupation when you were born? (title).....

0. Unemployed
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces
8. Student
9. Retired

92) If you are not the head of the household (and if applicable), what is the occupation of the head the household that you live in?

0. Unemployed
1. Professional
2. Intermediate occupations
3. Skilled occupations (non-manual)
4. Skilled occupations (manual)
5. Partly skilled
6. Unskilled occupations
7. Armed forces
8. Student
9. Retired

CONFIDANTS/ SUPPORT NETWORK

93) How often do you visit or speak to friend(s)/neighbour(s)/ work associates outside of work?

1. Visit/Speak to daily
2. Visit/Speak to weekly
3. Visit/Speak to fortnightly
4. Visit/Speak to monthly
5. < than above
0. Never

LIST MAIN FRIENDS/PEOPLE SEEN/SPOKEN TO REGULARLY

.....

.....

.....

94) *[If applicable]* Do your friends live close to you?

0. No
1. Yes locally (same area)
2. Yes (same town)

95) How often to you visit/ speak to your close family (including in-laws)?

1. Visit/Speak to daily
2. Visit/Speak to weekly
3. Visit/Speak to fortnightly
4. Visit/Speak to monthly

LIST FAMILY MEMBERS SEEN/SPOKEN TO REGULARLY

.....

.....

.....

.....

96) Do your close family live near you?

0. No
1. Yes (same are)
2. Yes (same town)

97) Do you have any close confidants?

1.Yes *0. No*

98) *If yes, who (check family and friends above).....*

.....

99) Would it have been the same person a year ago?

1.Yes *0. No*

100) If no, then who? .....

101) How often do you visit/ speak to your confidants?

1. Visit/Speak to daily
2. Visit/Speak to weekly
3. Visit/Speak to fortnightly
4. Visit/Speak to monthly
5. < than above

LIST CONFIDANTS SEEN/SPOKEN TO REGULARLY

.....
.....
.....
.....

102) If you had a worrying/ upsetting problem who would you discuss it with first?

1. Partner *2. Parent*
3. Sibling *4. Other relative*
5. Friend- female *6. Friend- male*
7. No one in particular *8. Don't share problems*

103) Anyone else?

1. Partner *2. Parent*
3. Sibling *4. Other relative*
5. Friend- female *6. Friend- male*
7. No one in particular *8. Don't share problems*

104) How helpful are they when you confide in them?

1. Very helpful *2. Fairly helpful*
3. Not very *4. Critical but truthful*
5. Too critical

105) What about emotional support and advice/listening

1. Very helpful *2. Fairly helpful*
3. Not very *4. Critical but truthful*
5. Too critical

106) How else do they help you? .....
.....
.....

107) Are you registered with a GP?

1. Yes *0. No*

108) [If no] is there any particular reason? .....

109) Would you go to the GP if you had a stressful problem?

1. Yes *0.No*

110) [If no] is there any particular reason? .....
.....

Appendix I Personal and Psychiatric History Schedule

PSYCHIATRIC AND PERSONAL HISTORY SCHEDULE 1

Starting Time: _____ **Finishing Time:** _____

Date of interview: 1-6

Centre No: 7,8

Interviewer ID No. 9,10

Resp. ID No: 11- 14

Date of admission 15-20

Section 21

Yes = 1
No = 0

Type of Section 22-23

2 = 1
3 = 2
4 = 3
5(2) = 4
5(4) = 5
37 = 6
37/41 = 7
47 = 8
48 = 9
136 =10

Sex of patient 24

1 = Male
2 = Female

Age of patient 25-26

Note: All dates are to be coded from the time of admission and not the time of this interview

For coding missing values in each field:-77 = Don't Know -88 = Refused to answer -99 = Not applicable

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Sources of information to fill in this form

0 - No
1 = Yes

Interview with the patient = 1
Key informant = 2
More than one informant = 3 [ ] 27

Case notes from previous or current admission [ ] 28

Other written documents (specify_____ [ ] 29
_____ _____ _____)

Other sources (specify_____ [ ] 30
_____ _____)

If a key informant was interviewed, specify:

(Note:- a key informant is a person who has been in daily or almost daily face-to-face contact with the patient

Relationship to patient [ ] 31

0 = Mother
1 = Father
2 = Spouse
3 = Other person living in the same household as patient
4 = Friend
5 = Other (specify_____ _____ _____)

8 = not applicable, no key informant available

Address (if different from patient's)_____

_____ _____ _____

Note: For coding missing values in each fields-77 = Don't Know -88 = Refused to answer -99 = Not applicable

If other informants (not qualifying as key informants) were interviewed, specify:

	Relationship to patient	Intensity of contact with patient in last three months 0 = low 1 = medium 2 = high or none
1.		
2.		
3.		
4.		
5.		

Locality where main interview with informants/patient took place: [ ] 32

0 = At research or hospital facility
1 = Patient's or informant's home
2 = Other (specify_____)
8 = Not applicable

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

INTRODUCTION TO INTERVIEW

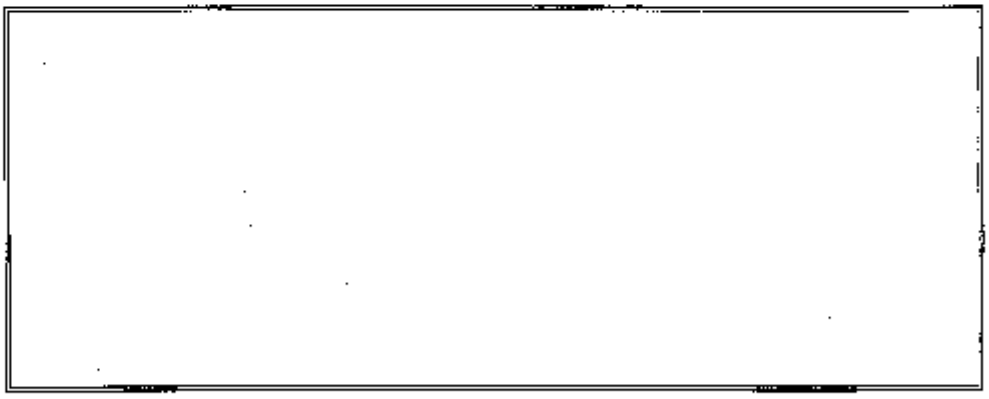
The investigator should first introduce himself/herself and thank the informant (or patient) agreeing to see the interviewer. The purpose of the interview should be explained briefly in approximately the following terms:-

> **"I work for... (Name of Institution or facility). We are now carrying out a scientific investigation about mental health problems with the aim of learning how to provide better medical care to people. I want to ask you a number of questions about yourself/X's health, about your/his/her past life, and about your family in general. I want to repeat that this is a scientific investigation and to assure you that everything you tell us about your/X will be treated confidentially and will not appear on any official hospital records".**

The investigator should satisfy himself that the informant (or patient) has understood these introductory words, and asked for the subject's explicit consent to proceed with the interview.

In every case of refusal of the interview, a note should be entered in the space provided below:

REASONS FOR INFORMANT'S (OR PATIENT'S) REFUSAL OF INTERVIEW



Note: For coding missing values in each field:-77 = Don't Know -88 = Refused to answer -99 = Not applicable

PART 1. PSYCHIATRIC HISTORY

"What, if anything, happened to make it necessary for X to come (to be brought to...) (Specify the hospital, clinic or other facility) at this particular time?" Cross-examine: "Was that the only reason?" "How serious was that?" "Which was the most important reason?" "Was there anything else?" *Try to obtain a description of behaviour or of an event if such has occurred. (The mode or agency of referral is not rated here but in item 1.6)*

1.1 ***RATE MAIN REASONS FOR CURRENT ADMISSION OR ATTENDANCE ACCORDING TO INFORMANT*** (rate as many as applicable).

0 = No
1 = Yes
8 = Not applicable or no information
9 = Uncertain

1.1.1	Patient attempted suicide or bodily harm	33
1.1.2	Patient's behaviour perceived as potential danger to himself (e.g. talked of killing or harming himself; refusal of food, etc).	34
1.1.3	Patient committed an assault, or other violent or hazardous act (e.g. setting fire or destroying property)	35
1.1.4	Patient's behaviour perceived by others as threatening or grossly annoying	36
1.1.5	Onset or exacerbation of odd behaviour, appearance or talk (e.g. excitement or withdrawal, self neglect, incoherent talk, bizarre ideas, loss of interest or abandoning work, wandering, marked anxiety or fears, etc)	37
1.1.6	Patient developed signs of physical illness or sustained an injury	39

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.1.7 Recent change of crisis in family or household necessitating contact without change of patient's condition (e.g. illness of a household member, rehousing, birth of a child, death of a household member, somebody getting married, etc) [ ] 39

1.1.8 Patient was referred for a routine checkup by a doctor or other health worker, or by an agency (e.g. school, driving licence authorities, etc) [ ] 40

1.1.9 Patient himself has requested admission or an appointment to see a doctor or other health worker because of complaints about his mental health (other than problems listed above) [ ] 41

1.1.10 Other reason (specify_____ [ ] 42

_____ _____

1.2 "You have already told me about the reason why X had to come to/ hospital, clinic, etc. - as relevant/ at this point in time, and about the kind of problems he has now. I should like now to ask you about things which happened in the past, mainly in the last year and maybe even earlier. What was it that made you aware for the first time ever that X was not behaving like his usual self? Did other people notice anything unusual about X's behaviour around that time; or maybe even earlier than you did?

Allow for informant to think and reply, then cross examine: "Was there nothing of the sort before that? Did that happen before or after.../use as a reference point in time a fact that the informant has already mentioned, or an event which should be locally known/ ?" *Write down a narrative note, in informant's own words, on first ever abnormality that he recollects, and its approximate timing:*

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.2 PROBABLE EARLIEST MANIFESTATION OF PATIENT'S ABNORMALITY PERCEIVED BY INFORMANT OR OTHERS

43-45

1.3 TIMING OF ABOVE EVENTS APPROXIMATE NUMBER OF MONTHS AGO (999 if unknown)

46-48

1.4 "Now I am going to ask you about other things that sometimes happen and may cause concern, and would like you to tell me if X did or experienced any of them after, or maybe even before..." / refer to event described under 1.2/. Interviewer goes over the checklist. If an informant gives an affirmative answer to question, interviewer should cross-examine as relevant, to establish the nature of the symptom or behaviour, and to estimate the time of its first occurrence or beginning. If as a result of cross-examination or other information, the interviewer establishes that a definite abnormality had occurred before the vent described in 1.2, he should record his own best estimate of timing of onset as required in 1.20/.

THE INTERVIEWER SHOULD MODIFY AS APPROPRIATE THE WORKING OF THE PROBES 1.4.1 - 1.4.26 IF THE INFORMANT IS THE PATIENT HIMSELF.

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.4 EARLY MANIFESTATIONS OF ABNORMALITY IN PATIENT

"DID X AT ANY TIME IN THE PAST...?	0 = No 1 = Yes 9 = Uncertain(99s	If yes, estimat No of months ag if impossible t estimate, 001 i less than one month ago!	
1.4 (1)	Show serious neglect of his usual activities at work or in the home, or marked loss of interest?		49-52
1.4 (2)	Persistently avoid the company of other people or refuse talking to them?		53-56
1.4 (3)	Lose all interest in personal appearance and cleanliness?		57-60
1.4 (4)	Lose his appetite, or sleep, or interest in sex?		61-64
1.4 (5)	Become very excited for days or weeks trying to do too many things at once?		65-69
1.4 (6)	Assault other persons physically?		69-72
1.4 (7)	Attempt to harm or kill himself?		73-76
1.4 (8)	Cause damage to property, e.g. destroy things or set fire?		77-80
1.4 (9)	Go away suddenly to another part of the country without giving good reason for doing so?		81-84
1.4 (10)	Spend many hours in a church or a temple when formerly he used to spend much less time there?		85-88

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.4 (11)	Get very irritable, quarrelsome or angry for days or weeks without sufficient reason?	89-92
1.4 (12)	Spend money in a wild and irresponsible fashion, quite unlike his former self?	93-96
1.4 (13)	Do anything inappropriate, indecent or annoying that would upset many people?	97-100
1.4 (14)	Talk incomprehensively, so that no one could understand what he wanted to say?	101-104
1.4 (15)	Behave on more than one occasion as if hearing voices when no one around was actually talking?	105-108
1.4 (16)	Say that he was being persecuted, harmed, or bewitched by other people? (Interviewer should fill in popular local contents of paranoid ideation)	109-112
1.4 (17)	Look very frightened or anxious for days or weeks without good reason?	113-116
1.4 (18)	Claim unlikely or impossible things, for example that God was talking to him, or people could read his thoughts, or everybody was talking about him, or people being not what they appeared to be, etc? (Interviewer should fill in local contents of delusional beliefs)	117-120

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.4 (19)	Look very sad, mournful or hopeless?	121-124
1.4 (20)	Say that he had lost his memory for a time so that he did not know where he was and what he was doing?	125-128
1.4 (21)	Talk about somebody who is dead as if that person was still alive?	129-132
1.4 (22)	Act as if he could not get a particular thought out of his head?	133-136
1.4 (23)	Complain persistently of various aches, pains or funny sensations in his body or head? (Interviewer should fill in popular local contents of morbid pre-occupations with own body)	137-140
1.4 (24)	Think he was suffering from an incurable illness while doctor (or other health worker) had said that nothing was wrong with his health?	141-144
1.4 (25)	Talk about great new plans he had for the future in a way he had never done before?	145-148
1.4 (26)	Do or say anything else out of the ordinary which I have not mentioned so far? Can you describe it and give me an example?	149-152

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.4 (27) ---------- ┌─┐ ┌─┬─┬─┐ 153-156
└─┘ └─┴─┴─┘

1.4 (28) ---------- ---------- ┌─┐ ┌─┬─┬─┐ 157-160
└─┘ └─┴─┴─┘

1.4 (29) ---------- - ┌─┐ ┌─┬─┬─┐ 161-164
└─┘ └─┴─┴─┘

Note: For coding missing values in each field:-77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.5 "You told me about some unusual things that X did or said, which made you think that he was not behaving like his former self. When you think of it, did this change in X develop quite suddenly, say within days, or slowly, over a longer period of time, maybe in weeks or even months? How about... /interviewer picks up examples of abnormal behaviour recorded under previous item/, did it start suddenly? Has X never before been like this/or said, done, etc./?"

1.5 RATE INFORMANT'S IMPRESSION OF MODE OF ONSET OF PATIENT'S DISORDER

1 = Clearly sudden onset, one or more psychotic symptoms appeared within days (up to a week); previous psychiatric symptoms can be safely excluded ┌─┐ 165 └─┘

2 = Precipitous onset of one or more psychotic symptoms within days, (up to a week) but previous existence of other non-psychotic symptoms likely or certain

3 = Acute onset, psychotic symptoms developed over a period of up to one month; previous psychiatric symptoms can be safely excluded

4 = Acute onset; psychotic symptoms developed over a period of up to one month; previous existence of other, non-psychotic symptoms likely or certain

5 = Insidious, slow incremental development of psychotic symptoms over many months

6 = Informant cannot draw a clear demarcation line between health and mental illness in the patient (no clear-cut psychotic symptoms described)

7 = Informant's description inadequate for making any judgement about mode of onset

8 = Question not asked

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.6 "Where did X/or informant/first go for help? Then where did X/or informant/next go for help?" */Interviewer continues in this manner until informant has enumerated all different sources of lay or professional help outside the household. Help from neighbours or relatives (unless they are professionally qualified) is not rated here. The last entry in the sequence of boxes below should refer to present treatment./*

Note: Rate only first contacts with a particular type of helping agent. For example, a patient who made three visits to two different traditional healers, then saw a general practitioner who referred him to a psychiatrist with whom the patient had two outpatient sessions, and then hospitalization during which he was treated by another psychiatrists, should be rated 5 2 1. A contact is a transaction between patient and helping agent which leads to some actions related to the management or treatment of a problem that in the rater's judgement was part of, or associated with the patient's mental illness.

1.6 *RECORD CONSECUTIVE CONTACTS WITH DIFFERENT HELPING AGENTS*

1st	2nd	3rd	4th	5th	6th	7th	
							156-172

1 = Psychiatrist or other mental health professional

2 = General practitioner or other medical specialist (non-psychiatric)

3 = Nurse, other health worker, or social worker

4 = Police

5 = Traditional healer or non-allopathic practitioner (include here homeopaths, naturopaths, acupuncturists, etc.
Specify_____

_____

6 = Priest or other religious person

7 = Other specify_____ _____

_____

8 = Unspecified (contact took place but type of agent unknown)

9 = Unknown

Note: For coding missing values in each field:-77 = Don't Know -88 = Refused to answer -99 = Not applicable

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Insert after 1.6 PPHS

Please write a narrative summary of the patient's pathway to contact with services, including all sources of help utilised by or offered to the patient since onset of symptoms and prior to contact with professional psychiatric services (family, friends, alternative therapies/healers, church, etc). Include details of who initiated help-seeking, and what the respondent and patient felt about the help offered.

1.7 "When did X go for help to.../ name the first contact recorded under the preceding item/. Cross-examine using a time frame of reference familiar to the informant and estimate the number of weeks that have elapsed since first contact.

1.7 ***RATE NUMBER OF WEEKS SINCE FIRST CONTACT WITH A HELPING AGENCY RELATED TO CURRENT MENTAL DISORDERS***

No. of weeks ago (999 if impossible to estimate) ┌┬┬┐ 173-175

1.8 "What do you believe is the matter with X?" "What do you think might have caused it?" Cross examine: "Can you tell me more about it? Could it be.../give example/? What do you think is the main problem?" *INTERVIEWER SHOULD AVOID SUGGESTING POSSIBLE ANSWERS TO THE INFORMANT. Code the conceptualization which informant considers most likely. Record actual words of informant.*

1.8 RATE INFORMANT'S OR PATIENT'S OWN CONCEPTUALIZATION OR NATURE OF PATIENT'S CURRENT PROBLEM

0 = No conceptualization, informant has no explanation ┌┐ 176

1 = Nothing wrong, problem denied

2 = Feels something is wrong but no specific problem described

3 = Problem seen as mental illness (e.g. "nerves", depression, schizophrenia, etc.)

4 = Problem seen as physical illness

5 = Problem seen as a spiritual, religious or a moral one (e.g. a "revelation", "pangs of conscience", etc)

6 = Magic, curse, taboo, etc.

7 = Unacceptable behaviour (e.g. lies in bed, won't work, poor habits, etc.) or motivation (e.g. lazy)

7a= Problem seen as aberrant/delinquent bad behaviour

7b= Problem seen as dangerous/evil

Note: For ending missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

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8 = Other specify_____

_____

9 = Not applicable

1.9 "What has... /psychiatrist, other doctor, healer, priest, social worker, or anyone else outside the family involved in the management of the present problems of the patient/told you is the matter with X?" *(Try to assess if conflicting opinions and advice were given by different persons; id so, rate as many explanations as relevant)*

1.9 ***RATE EXPLANATION OF NATURE OF PATIENT'S PROBLEM AS GIVEN TO INFORMANT OR PATIENT BY OUTSIDE AGENCIES***

0 = No
1 = Yes

If no outside agencies involved up to the present moment, fill in 8's?

1.9.1	No explanation given	177
1.9.2	Was told nothing was wrong, problem denied	178
1.9.3	Was told something was wrong but no specific nature of the problem outlined	179
1.9.4	Mental illness (e.g. "nerves", depression, schizophrenia, etc)	180
1.9.5	Problem explained in terms of physical illness or illness or physical/mental interaction	181
1.9.6	Problem explained in spiritual, religious or moral terms	182
1.9.7	Magic, curse, taboo, etc	183
1.9.8	Problem explained as unacceptable behaviour (e.g. habits) or motivation	184

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.9.8a Problem seen as aberrant/delinquent bad behaviour ☐ 185

1.9.8b Problem seen as dangerous/evil ☐ 186

1.9.9 Other, (specify)_____ ☐ 187

_____

1.10 "What do you think may have caused the problem? Anything else? What is the main cause?" Probe and cross-examine: "Can you tell me more about it? Could it be.../give examples/?

1.10 RATE INFORMANT'S EXPLANATION OF THE CAUSE OF PATIENT'S CURRENT PROBLEM

0 = No
1 = Yes
8 = Not applicable or not inquired;
9 = Uncertain

1.10.1 No explanation, informant cannot identify any specific cause ☐ 188

1.10.2 Cause seen in heredity (e.g. "born that way", "got if from his mother", "his uncle was like that", etc.) ☐ 189

1.10.3 Cause seen in faulty biological functioning due to disease, brain disturbance or injury (e.g. "had malaria", "fell on his head", etc.) ☐ 190

1.10.4 Cause seen in substance abuse (e.g. "drinks too much", "had marijuana", "smokes too much", etc.) ☐ 191

1.10.5 Cause seen in faulty nutritional habits (e.g. undernourishment, eating too much or too little of a particular food, etc.) ☐ 192

1.10.6 Cause seen in physical effects of environment (e.g. "heat", "bad air" etc.) ☐ 193

Note: For coding missing values in each fields-77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.10.7 Cause seen in intimate interpersonal relationships or family life (e.g. "unhappy family life", "spouse ruined his/her health", "love disappointment", etc.) [ ] 196

1.10.8 Cause seen in patient's character, or lifestyle (e.g. "bad apple", "worries too much", "overwork", "fatigue", "stress", "too much sex", "no sex", etc.) [ ] 195

1.10.9 Cause seen in social environment (e.g. "cultural deprivation", "social class", "social change", "migration", etc.) [ ] 196

1.10.10 Cause seen in supernatural forces (e.g. "bewitchment", "spirits", "evil eye", etc.) unprovoked by patient [ ] 197

1.10.11 Cause seen in supernatural forces (e.g. "bewitchment", "spirits", God's wrath, etc.) provoked by patient through breaking of taboo [ ] 198

1.10.12 Cause seen in specific precipitating event of special significance (e.g. "saw a snake and panicked") [ ] 199

1.10.13 Other cause (specify)_____ [ ] 200

_____

1.10.14 **"How much do you hold the patient responsible for the condition?**

1.10.14 Rate degree of patient's own responsibility or control over cause of disorder according to informant [ ] 201

0 = No responsibility or control
1 = Partial responsibility or control
2 = Total responsibility or control
8 = Not applicable or not inquired
9 = Uncertain

Please write a brief narrative about cause(s) as perceived by informant _____

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

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1.15 **"Could you tell us something about X's drinking habits? Do you think that X drinks too much? During the past one year has X had any of the following problems, because of drinking?"** */Inquire about family tension, job difficulties, trouble with the law, physical symptoms or illnesses, accidents, etc. - due to use of alcohol./*

1.15 ***RATE ALCOHOL USE IN LAST YEAR*** [ ] 202

0 = None at all
1 = Only occasional social drinking
2 = Moderate use of alcohol
3 = Serious alcohol problem suspected
4 = Clear evidence of serious alcohol problem
9 = Not known

1.16 *Do not ask if excessive or regular use of alcohol denied by informant./* **"Has X ever had any treatment for a drinking problem?"**

1.16 ***RATE TREATMENT FOR ALCOHOL PROBLEM IN THE PAST*** [ ] 203

0 = No
1 = Yes (specify what treatment and when)

8 = Not applicable, no evidence of excessive or regular use of alcohol
9 = Not known

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

1.17 "Do you know if X has ever taken drugs like hashish, 'pep pills'/enumerate any other drugs using their locally known names/for pleasure, or to get more strength, or to calm him down? What was it? When? How often? How did he feel? Do you think he might have been taking it more often than you know?"

RATE DRUG-TAKING IN LAST YEAR 204

0 = Drug-taking in last year can be safely excluded
1 = Drug-taking suspected only
2 = Sporadic/up to 3 - 4 times/ drug-taking in last year known, no reason to suspect more frequent abuse
3 = Sporadic drug-taking in last year known, but there are reasons to suspect that more frequent abuse actually occurred
4 = Five or more instances of drug-taking known
8 = Question not asked
9 = No information obtained from informant

IF RATING OF EITHER 2, 3 OR 4 MADE ABOVE, INTERVIEWER SHOULD ATTEMPT TO ELICIT INFORMATION ABOUT THE NATURE OF THE SUBSTANCE(S) TAKEN

0 = No
1 = Yes
8 = Not applicable or not inquired
9 = Uncertain

1.17.1	Morphine or Heroin	205
1.17.2	Opium or Derivatives	206
1.17.3	Amphetamines or Derivatives	207
1.17.4	Hashish or Marijuana	208
1.17.5	Hallucinogens (LSD and others)	209
1.17.6	Cocaine	210
1.17.7	Barbiturates	211
1.17.8	Non-barbiturates sedatives and tranquillizers	212
1.17.9	Other (specify_____ _____)	213

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

 AESOP 2.9.97

1.18 *Do not ask if no evidence of drugs use.*

"Has X had any treatment for a drug problem?"

RATE TREATMENT FOR DRUG PROBLEM IN THE PAST

214

0 = No
1 = Yes (specify what treatment and when_____
_____ _____ _____

9 = Not applicable, no evidence of drug use
9 = Not known

1.19 **"I want now to ask you a question we ask routinely of everybody: has X ever had any kind of trouble with the law, or the Police?"** */If reply suggestive of a possibility of past contacts with the law, probe further about arrests, detection in an institution, probation, etc., and obtain details to fill in the following chart./*

1.19 HISTORY OF CONTACTS WITH THE LAW BECAUSE OF OFFENCE(S)

0 = No
1 = Yes
8 = Uncertain
9 = Not known

1.19.1	Arrested	215
1.19.2	Detained in an institution ie hospital Please state	216
1.19.3	Probation	217

Note: For coding missing values in each field:-77 = Don't Know -88 = Refused to answer -99 = Not applicable

IF RATED POSITIVE ABOVE, FILL IN DETAILS:

Date of charge or arrest	A. Nature of offence or charge	B. Verdict and sentence (if any)	C. Type of institution in which sentence if any, was served	D. Time in institution or on probation

1.20 ON THE BASIS OF ALL INFORMATION AVAILABLE ESTIMATE THE NUMBER OF MONTHS SINCE THE ONSET OF THE CURRENT MENTAL DISORDER IN THIS PATIENT

(Re-rate this item at end of interview, at any other time if additional data necessitates this.)

218-220

No. of months
(999 if impossible to estimate)

Note: For coding missing values in each fields-77 = Don't Know -88 = Refused to answer -99 = Not applicable

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RESIDENCE

In order to make the rating specified in this section, use the questions as appropriate; cross examine and ask for examples if necessary. No special wording of the questions in this section is suggested.
Current address of patient

How long at this address 221

How many people live at this address 222

RATE TYPE OF COMMUNITY
0=urban
1=peri-urban or suburban
2=rural
3=other (specify_____) 223
4=not known

RATE PATIENTS LIVING ARRANGEMENTS
0=own flat or house (owned by patient or his / her family)
1=rented apartment or house (self contained)
2=rented room(s) only in a flat or house share with other people; bedsitter
3=hostel or equivalent 224
4=no fixed abode or vagrant
5=other (specify)

NUMBER OF ROOMS IN CURRENT DWELLING 225

NUMBER OF PEOPLE LIVING IN CURRENT DWELLING 226

ENQUIRE ABOUT THE PLACE OF BIRTH OF THE PATIENT
0 = within the catchment area of this study
1 = within a 50km radius of catchment area of this study
2 = within this country (main national boundaries) 227
but outside 50km radius specify town/village and district
3 = outside of this country (specify country)

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

IF PATIENT BORN OUTSIDE OF THIS COUNTRY RATE AGE OF MIGRATION
1 = below age 18
2 = age 18 and above
8 = not applicable
9 = not known

228

Specify date

229-234

ENQUIRE ABOUT BIRTHPLACE OF BIOLOGICAL MOTHER

0 = within the catchment area of this study
1 = within a 50km radius of catchment area of this study
2 = within this country (main national boundaries)
but outside 50km radius specify town/village and district
3 = outside of this country (specify country)
9 = Not known

235

If mother born outside the UK specify date of migration

236-241

Date of birth for biological mother

242-247

ENQUIRE ABOUT BIRTHPLACE OF BIOLOGICAL FATHER

0 = within the catchment area of this study
1 = within a 50km radius of catchment area of this study
2 = within this country (main national boundaries)
but outside 50km radius specify town/village and district
3 = outside of this country (specify country)
9 = Not known

248

If father born outside the UK specify date of migration

249-254

Date of birth for biological father

255-260

Note: For coding missing values in each field:-77 = Don't Know -88 = Refused to answer -99 = Not applicable

PART 10 - OCCUPATION

10.11 Estimate the degree of prestige (status) of patient's last job in the community

10.11 RATE SOCIAL PRESTIGE OF PATIENT'S JOB

0 = Low
1 = Average
2 = High
3 = Impossible to estimate
8 = Not applicable (specify reason_____

_____ 261

10.12 Is the patient's occupational level in last job the same as his/her highest level in any job before last?

10.12 RATE UPWARD/DOWNWARD CHANGE IN OCCUPATIONAL LEVEL

0 = The same or higher
1 = Lower
2 = Not applicable, patient never employed or started working less than a year ago
3 = Not known

262

10.12 Consider: (i) patient's ability to conform to the work routine - going to work regularly and on time, observing the rules, etc; (ii) quality of performance and output. (Household work excluded).

10.13 RATE WORK PERFORMANCE IN JOB IN LAST YEAR

0 = Patient goes to work regularly; output and quality of performance within levels expected for job

263

1 = Compared with the average employee in same type of job or in same place, the patient has been absent from work more often, or there has been a decline in his/her output and quality of performance; or patient has complained persistently that work is too heavy for him/her. If above description applies to a sheltered job, rate 2
2 = Patient has been absent from work most of the time; or has been fired because of poor performance; or has shown more than once gross neglect at work
9 = Not applicable, e.g., patient not working or a house-wife

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

10.14 *RATE PERFORMANCE IN HOUSEHOLD WORK IN LAST YEAR*

0 = No change in comparison to previous years
1 = Some deterioration
2 = Marked deterioration
5 = Improvement
8 = Not applicable, patient never did household work
9 = Not known

264

PART II - EDUCATION

11.1 **"What is the highest level of completed education the patient has achieved?"**

11.1 *RATE PATIENT'S LEVEL OF EDUCATION*

0 = No schooling or unfinished primary school
1 = Finished primary school (e.g. 4-5 years of completed education)
2 = Finished secondary school or equivalent (e.g. technical or occupational)
3 = Finished school intermediary between secondary school and university (wherever applies)
4 = Finished university
7 = Finished other school (specify_____)
9 = Not known

265

11.2 **"Has the patient been a student during the past one year?"**

11.2 *STUDYING DURING PAST YEAR*

0 = No
1 = Yes, full-time student
2 = Yes, part-time student and part-time working
3 = Yes, part-time student and full-time working
4 = Yes, full-time student and full-time working
5 = Has been a student for some time but then discontinued
9 = Not known

266

11.3 **"If patient has been a student during past year, what kind of education was he receiving?"**

Note: For coding missing values in each field:-77 = Don't Know -88 = Refused to answer -99 = Not applicable

11.3 *NATURE OF STUDY DURING PAST YEAR*

0 = General (e.g. reading, writing, arithmetic) ┌─┐
1 = Specialized - training for a trade or apprenticeship (specify_____) 267 └─┘
2 = Specialized - academic (specify nature of course _____ _____ _____

8 = Not applicable, patient was not a student
9 = Not known

11.4 *RATE WORK (STUDY) PERFORMANCE IN LAST YEAR IF PATIENT WAS A STUDENT*

0 = Excellent ┌─┐
1 = Fair 268 └─┘
2 = Poor
8 = Not applicable, patient was not a student
9 = Not known

PART 12 - RELIGION

12.1 "Does patient belong to any particular religious group or church?"

12.1 *RATE PATIENT'S RELIGIOUS AFFILIATION (REGARDLESS OF ACTIVITY)*

0 = None ┌─┐
1 = Yes (specify religion or denomination 269 └─┘
_____
9 = Not known

12.2 "has patient shown any active interest in religion during the past year"?

12.2 *RATE CURRENT DEGREE OF RELIGIOUS ACTIVITY*

0 = None at all ┌─┐
1 = Observed some rituals or festivities but not more active than average from his cultural and social group 270 └─┘
2 = Much more active than average for his cultural and social group
8 = Not applicable
9 = Not known

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

14.3 "Now I would like to ask you about the sort of person X was as an adult, up to the moment when his behaviour changed/or present illness started".

14.3 *RATE PATIENT'S ADULT PRE-MORBID PERSONALITY TRAITS*

The characteristics listed below should have been present for at least several years before the onset of the illness. This makes it difficult to rate pre-morbid personality in patients whose illness began in early adolescence

14.3 "AS A GROWN-UP PERSON, (BUT BEFORE ONSET OF ILLNESS), DID THE PATIENT?"

0 = Absent or not present in any marked degree
1 = Present in marked degree
2 = Uncertain
8 = Not applicable
9 = Not known (not asked)

14.3.1	Appear to be generally suspicious of other people's intentions?	271
14.3.2	Often complain that people were picking on him?	272
14.3.3	Show excessive jealousy?	273
14.3.4	Show marked lack of self-criticism, or inability to see his own fault when he did something wrong?	274
14.3.5	Seem to be generally gloomy and pessimistic about the future?	275
14.3.6	Appear to be generally excited and energetic?	276
14.3.7	His mood go up and down all the time?	277
14.3.25	Have set routine or fixed habits which he had to keep or else got upset?	270

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

14.3.26	Seem to be considered in the community to be an eccentric?	279
14.3.27	Impress others as being emotionally cool and withdrawn?	280
14.3.28	Have a tendency to exaggerate facts or confabulate?	281
14.3.29	Appear to be always optimistic and hopeful about the future?	282
14.3.30	Show a very marked capacity to endure stress?	283
14.3.31	Show dependability, loyalty, and reliability in social relations?	284
14.3.32	Demonstrate marked independence and autonomy in judgements and decisions?	285

Please write in a brief narrative of your impressions of the patient's pre-morbid personality (optional):

THE END

Note: For coding missing values in each field: -77 = Don't Know -88 = Refused to answer -99 = Not applicable

Appendix J Childhood Experience of Care and Abuse Questionnaire

ÆSOP

FAMILY RELATIONSHIPS IN CHILDHOOD

CECA-Q

Name …….. ….. …….. Date……

ÆSOP case/control ID ☐ ☐ ☐ ☐ ☐

This questionnaire is part of a research survey concerning aspects of childhood.
We are equally interested in people with TYPICAL or ATYPICAL experiences.

We would be very grateful if you could fill in *all* of the following questions about yourself.

Your replies will be treated in the strictest confidence.

1. WHO BROUGHT YOU UP BEFORE AGE 17

Please write below the *Parent Figures* who brought you up in childhood. List each family arrangement with different parent figures which lasted *one year or longer*.
Consider natural parent, step-parent (including parent's live-in partner), aunt, friend of the family, adoptive parent, foster parent etc.

Fill in the first family arrangement below. For example, if this was with your natural parents, write in 'Mother' and 'Father' and age '0'; or if this was with just your mother write in 'Mother', put 'No father figure' in the father column, and age '0'.

Family arrangement	**Mother figure**	**Father figure**	**Your age at start**
FIRST family	1a	1b	1c

If this was your *only* family up to the age of 17, then SKIP to the starred question below.

If you have lived in *more than just one* family arrangement, such as with mother and stepfather, then list them below, together with the age you were when the arrangement began.

Family arrangement	**Mother figure**	**Father figure**	**Your age at start**

SECOND family	1d	1e	1f
THIRD family	1g	1h	1i
FOURTH family	1j	1k	1l
FIFTH family	1m	1n	1o

1p ****Were you ever in a children's home or institution before age 17? YES NO**
(please circle the appropriate answer)

If 'YES' fill in the boxes below. If 'NO' skip to question 2 overleaf

TYPE OF INSTITUTION **e.g. local authority care, hospital, boarding school**	**age when you started**	**age when you left**
1st (1q)	1r	1s
2nd (1t)	1u	1v

2. PARENTAL LOSS

Please circle the appropriate answers, and write in the age you were when it happened.

	MOTHER	**FATHER**
2a. Did either parent die before you were aged 17?	YES NO	YES NO
If YES, what age were you?	2b	2c

	MOTHER	**FATHER**
2d. Have you ever been separated from your parent *for one year or more* before the age of 17?	YES NO	YES NO

If YES, then fill in the boxes below; if NO then SKIP to question 3 overleaf.

	MOTHER	**FATHER**
At what age were you first separated?	2e	2f
How long was this separation, in years?	2g	2h
Please circle the reason for the separation:		
Parent's illness (2i)	YES NO	YES NO
Parent's work (2j)	YES NO	YES NO
Parents' divorce or separation (2k)	YES NO	YES NO
Abandoned by parent or never knew parent (2l)	YES NO	YES NO
Other reason (2m)	YES NO	YES NO

2n. Please describe your experience…….

……..

…….

3. Please circle the appropriate numbers to describe your **Mother Figure, as you remember her in your first 17 years**. If you had more than one, choose the one you were with *the longest*, or the one you found *most difficult* to live with.

3a. Which mother figure are you describing below?

1. Natural mother
2. Step-mother/father's live-in partner
3. Other relative e.g aunty, grandmother
4. Other non-relative e.g. foster mother, godmother
5. Other (describe)……

	Yes, definitely		Unsure		No, not at all
3b She was very difficult to please	1	2	3	4	5
3c She was concerned about my worries	1	2	3	4	5
3d She was interested in how I did at school	1	2	3	4	5
3e She made me feel unwanted	1	2	3	4	5
3f She tried to make me feel better when I was upset	1	2	3	4	5
3g She was very critical of me	1	2	3	4	5
3h She would leave me unsupervised before I was 10 years old	1	2	3	4	5
3i She would usually have time to talk to me	1	2	3	4	5
3j She would hit me	1	2	3	4	5
3k At times she made me feel I was a nuisance	1	2	3	4	5
3l She often picked on me unfairly	1	2	3	4	5
3m She was there if I needed her	1	2	3	4	5
3n She was interested in who my friends were	1	2	3	4	5
3o She was concerned about my whereabouts	1	2	3	4	5
3p She cared for me when I was ill	1	2	3	4	5
3q She neglected my basic needs (e.g. food and clothes)	1	2	3	4	5
3r She did not like me as much as my brothers and sisters (*leave blank if no siblings*)	1	2	3	4	5

3s. Do you want to add anything about your mother?……..
……..

4. Please circle the appropriate numbers to describe **your Father Figure, as you remember him in your first 17 years**. If you had more than one, choose the one you were with *the longest*, or the one you found *most difficult* to live with.

4a. Which father figure are you describing below?

1. Natural father
2. Step-father/mother's live-in partner
3. Other relative e.g uncle, grandfather
4. Other non-relative e.g. foster father, adoptive father
5. Other (describe)……

	Yes, definitely		Unsure		No, not at all
4b He was very difficult to please	1	2	3	4	5
4c He was concerned about my worries	1	2	3	4	5
4d He was interested in how I did at school	1	2	3	4	5
4e He made me feel unwanted	1	2	3	4	5
4f He tried to make me feel better when I was upset	1	2	3	4	5
4g He was very critical of me	1	2	3	4	5
4h He would leave me unsupervised before I was 10 years old	1	2	3	4	5
4i He would usually have time to talk to me	1	2	3	4	5
4j He would hit me	1	2	3	4	5
4k At times he made me feel I was a nuisance	1	2	3	4	5
4l He often picked on me unfairly	1	2	3	4	5
4m He was there if I needed him	1	2	3	4	5
4n He was interested in who my friends were	1	2	3	4	5
4o He was concerned about my whereabouts	1	2	3	4	5
4p He cared for me when I was ill	1	2	3	4	5
4q He neglected my basic needs (e.g. food and clothes)	1	2	3	4	5
4r He did not like me as much as my brothers and sisters (*leave blank if no siblings*)	1	2	3	4	5

4s. Do you want to add anything about your father?……

……..

5. CLOSE RELATIONSHIPS IN CHILDHOOD
(please circle as appropriate – if you circle NO to any question, SKIP the rest of that section and go on to the next one)

5a When you were a child or teenager, were there any ADULTS you could go to with your problems or to discuss your feelings?

YES NO

5b If YES: Who was that? (circle more than one if relevant)

1. mother / mother figure
2. father / father figure
3. other relative
4. family friend
5. teacher, vicar etc
6. other (describe) ……..

5d Do you want to note anything about the relationship(s)? ……

5e Were there other CHILDREN/TEENAGERS your age that you could discuss your problems and feelings with?

YES NO

5f If YES: Who was that? (circle more than one if relevant)

1. sister
2. brother
3. other relative
4. close friend
5. other less close friend(s)
6. other person (describe)……..

5h Do you want to note anything about the relationship(s)?……

5i Who would you describe as the TWO CLOSEST people to you as a child/teenager? (circle up to two)

1. mother / mother figure
2. father / father figure
3. sister or brother
4. other relative
5. family friend (adult)
6. friend your age
7. other (describe) …….

5k Do you want to note anything about the relationship(s)?……

6. PHYSICAL PUNISHMENT BEFORE AGE 17 BY PARENT FIGURE OR OTHER HOUSEHOLD MEMBER

6a When you were a child or teenager were you ever hit repeatedly with an implement (such as a belt or stick) or punched, kicked or burnt by someone in the household?

YES NO

If YES, then fill in the boxes below; if NO then SKIP to question 7 overleaf.

	MOTHER FIGURE	**FATHER FIGURE**
How old were you when it began, in years?	6b	6c
Did the hitting happen on more than one occasion?	6d YES NO	YES NO
How were you hit?	6e 1. belt or stick 2. punched/kicked 3. hit with hand 4. other	6f 1. belt or stick 2. punched/kicked 3. hit with hand 4. other
Were you ever injured e.g. bruises, black eyes, broken limbs?	6g YES NO	YES NO
Was this person so angry they seemed out of control?	6h YES NO	YES NO

6i. Can you describe these experiences ……..

…….

…….

6j. Did you experience this from anyone else in the household? YES NO

6k. If YES: describe your experiences…….

…….

…….

7. UNWANTED SEXUAL EXPERIENCES BEFORE AGE 17
(please circle as appropriate)

7a. When you were a child or teenager did you ever have any unwanted sexual experiences? **YES NO UNSURE**

7b. Did anyone force you or persuade you to have sexual intercourse against your wishes before age 17? **YES NO UNSURE**

7c. Can you remember any upsetting sexual experiences **before age 17 with a related adult or someone in authority e.g. a teacher?** YES NO UNSURE

If NO to all these, then SKIP to question 8 overleaf
If YES or UNSURE to any of them, then please complete the following questions:

	FIRST EXPERIENCE	**SECOND EXPERIENCE**
What age were you when it began (in years)?	7d	7e
Was the other person someone you knew?	7f YES NO	YES NO
Was the other person a relative?	7g YES NO	YES NO
Did the other person live in your household?	7h YES NO	YES NO
Did this person do it to you on more than one occasion?	7i YES NO	YES NO
Did it involve touching private parts of your body?	7j YES NO	YES NO
Did it involve touching private parts of the other person's body?	7k YES NO	YES NO
Did it involve sexual intercourse?	7l YES NO	YES NO

7m. Can you describe these experiences?……

…….

……..

8. YOUR CURRENT RELATIONSHIPS AND WORK

(Please circle or write in your answer – if you circle NO to any question, SKIP the rest of that section and go on to the next one)

8a. Do you have a partner? YES NO

If YES:

8b. Are your currently living with your partner?

0. No
1. Yes, cohabiting
2. Yes, married

8c. Does your partner work?

0. No
1. Student only
2. Part-time employment
3. Full-time employment

8d. What is your partner's job? ……..

8e. Do you have children? YES NO EXPECTING FIRST BABY

If YES:

8f. How many children do you have? ……

8g. How many are currently living with you? …….

8h. How old is your eldest child?…….

8i. How old is your youngest child?…….

8j. Do any of your partner's children live with you YES NO
(i.e. your step-children)

8k Are you currently employed?

0. No
1. Student only
2. Part-time employment
3. Full-time employment

8l. If YES, what is your job? …….

8m. Your gender: MALE FEMALE

8n. Your current age ……

Thank you for your help with this questionnaire. We realise that it is difficult to give a true picture of your childhood experience in a questionnaire, so if you have any comments you would like to add, please write them below. Your responses will be treated in the strictest confidence.

Appendix K Life Events and Difficulties Schedule

Five Year Events and Difficulties Checklist

Starting Time: _____ **Finishing Time:** _____

Date of interview: **Centre No**:

Interviewer ID No. **Resp ID No.**

Having recently spent time talking about the past year, we are also interested in any experiences or events that have happened prior to the past year (but within the past five years) which have involved: *yourself, your partner, your children, other family members and close friends.*

Listed below are a number of events. If you have experienced any events of that nature could you indicate approximately the month and year in which it occurred.

Could you also indicate whether any of these experiences have occurred because of your: (appearance/colour/ethnicity/religion/etc **(as appropriate**)?

Coding relationship to respondent:

Spouse/ Partner	= 1	*Children*	=2	*Mother*	=3
Father	= 4	*Sibling*	=5	*Grandparent*	=6
Close Friends	= 7	*Friends*	=8	*Other*	=9

SECTION I HEALTH/ ILLNESS	**Rel**	**Yes/No**	**Year and Month**
1. Onset of a serious illness in you, your partner or your children	**……..**	**……..**	**……**
2. Accident causing serious injury to you, your partner or your children	**……..**	**……..**	**……**
3. A death in your household or immediate family	**…….**	**……..**	**……...**
4. Unwanted pregnancy- to you, your Partner or any of your children	**……..**	**……..**	**……**
5. Have you, your partner or any of your children had an abortion, a miscarriage, stillbirth or child born with serious health problems	**……..**	**……**	**……...**

Could you indicate whether any of these experiences have occurred because of your *appearance/colour/ ethnicity/religion etc (as appropriate)?*

……..

SECTION IV	HOUSING	Rel	Yes/No	Year and Month
6.	**A major disappointment for you such as an application for rehousing or a loan being rejected**	**……**	**……..**	**……**

Could you indicate whether any of these experiences have occurred because of your a*ppearance/colour/ ethnicity/religion etc (as appropriate)?*

……..

SECTION V	EMPLOYMENT	Rel	Yes/No	Year and Month
7.	**Loss of a job or retirement to you or anyone else in your household**	**……**	**…….**	**……**

Could you indicate whether any of these experiences have occurred because of your *appearance/colour/ ethnicity/religion etc (as appropriate)?*

……..

SECTION VII	MARITAL/ COHABITING	Rel	Yes/No	Year and Month
8.	**A serious row or rift with your spouse/ partner**	**…….**	**……**	**……..**
9.	**A serious row or rift with someone in the immediate family or with whom you felt very close**	**……..**	**…….**	**……..**

Could you indicate whether any of these experiences have occurred because of your *appearance/colour/ ethnicity/religion etc (as appropriate)?*

……..

SECTION X	CRISES	Rel	Yes/No	Year and Month
10.	**A serious breach of the law by you Your partner or your children**	**…….**	**……**	**……...**

Could you indicate whether any of these experiences have occurred because of your *appearance/colour/ ethnicity/religion etc (as appropriate)?*

……..

ONGOING DIFFICULTIES		Rel	Yes/No	Year and Month
11.	**Any news of a shocking or revealing nature about your partner or your children**	**…….**	**……**	**……..**
12.	**Serious chronic illness- yours, your spouse/partner, your children's or anyone else in the household**	**……..**	**…….**	**……...**
13.	**Serious problems with your children**	**……..**	**…….**	**……...**

14.	**Serious financial difficulties**	**……..**	**…….**	**……...**
15.	**Problems concerning unemployment - yours or your spouse/ partner's**	**……..**	**…….**	**…….**
16.	**Describe below any other particularly unpleasant or disappointing event or difficulty that has occurred.**	**……..**	**…….....**	**……**

Could you indicate whether any of these experiences have occurred because of your *appearance/colour/ ethnicity/religion etc (as appropriate)?*

……..

Appendix L Family Interview for Genetic Studies

FIGS FAMILY TREE

This page left intentionally blank for Family Tree to include first degree relatives with date of birth, gender, and place of birth

FIGS GENERAL SCREENING QUESTIONS

INTERVIEWER: Before you begin, you need to generate or obtain a family tree, with date of birth and gender, on which to record all of the responses to the following General Screening Questions. (See FIGS Manual for details.)

Step 1: *Let's go over your family.* (Include parents, siblings and offspring aged 18 or above)

Step 2: *Now I am asking you to keep in mind all those in your family as I go through this list of questions.* (Note all positive responses on the pedigree.)

Did anyone:

Feel very low for a couple of weeks or more, or have a diagnosis of depression?

Attempt or complete suicide?

Seem overexcited (or manic) day and night, or have a diagnosis of mania?

Have visions, hear voices, or have beliefs that seem strange or unreal?

Have unusual or bizarre behavior, or have a diagnosis of schizophrenia?

(Was anyone) hospitalized for psychiatric problems?

Step 3: For each of these given a positive response in the General Screening, complete the symptom checklist for any suspected: Depression/Mania, Psychosis, or Paranoid/Schizoid/Schizotypal Personality.

DEPRESSION

Code for a single episode (best recalled, worst episode if possible).

		No	Yes	Unk
1.	*During depression…*			
1.a)	*…was he/she depressed most of the day, nearly every day, for as long as a week or more?*	0	1	9
1.b)	*…did he/she lose interest in things or become unable to enjoy most things, for as long as a week?*	0	1	9
1.c)	*…did he/she have a change in appetite or weight without trying to?*	0	1	9
1.d)	*…did he/she have a change in sleep patterns (either too much or too little)?*	0	1	9
1.e)	*…did he/she become unable to work, go to school, or take care of household responsibilities?*	0	1	9

If yes: Describe: _____

_____

Discontinue this checklist

1.f)	*…did he/she move or speak more slowly than usual?*	0	1	9
1.g)	*…did he/she pace or wring his/her hands?*	0	1	9
1.h)	*…did he/she have less energy or feel tired out?*	0	1	9
1.i)	*…did he/she feel guilty, worthless or blame himself/herself?*	0	1	9
1.j)	*…did he/she have trouble concentrating or making decisions?*	0	1	9
1.k)	*…did he/she talk of death or suicide? Or try suicide?*	0	1	9
1.l)	*…did he/she have visions, or hear voices, or have beliefs or behavior that seem strange or unusual, at the same time as (symptoms above)?* (**If YES**, complete a Psychosis Checklist after this one.)	0	1	9

Code Response

2. Code and describe professional treatment: 0 1 2 3 4 9

   0. None
   1. Inpatient: _____
   2. Outpatient: _____
   3. ECT: _____
   4. Medication: _____
   9. Unknown

Age

3. Age of onset

Episodes

4. Number of episodes

Weeks

5. Duration of longest episode in weeks

Code Response

6. Rate and code impairment or incapacitation: 0 1 2 3 4 9

   0. None
   1. Modified RDC Impairment
   2. Modified RDC Incapacitation
   3. RDC Minor Role Dysfunction
   4. Change from previous functioning
   9. Unknown

7. Interviewer judgment on reliability of this information: 1 2 3

   1. Good
   2. Fair
   3. Poor

MANIA

		No	Yes	Unk
1.	*For most of the time day and night over several days, did he/she (more than usual)…*			
1.a)	*…seem too happy/high/excited?*	0	1	9
1.b)	*…become so excited or agitated it was impossible to converse with him/her?*	0	1	9
1.c)	*…act very irritable or angry?*	0	1	9
1.d)	*…need less sleep without feeling tired?*	0	1	9
1.e)	*…show poor judgement (e.g., spending sprees, sexual indiscretions?)*	0	1	9

If yes: Describe: _____

_____

Discontinue this checklist

1.f)	*…behave in such a way as to cause difficulty for those around him/her* (obnoxious/manipulative)?	0	1	9
1.g)	*…feel that he/she had special gifts or powers?*	0	1	9
1.h)	*…become more talkative than usual?*	0	1	9
1.i)	*…jump from one idea to another?*	0	1	9
1.j)	*…become easily distracted?*	0	1	9
1.k)	*…get involved in too many activities at work or school?*	0	1	9
1.l)	*…have visions? Hear voices? have beliefs or behavior that seem strange or unusual? at the same time as (above symptoms)?* (If YES, complete a Psychosis Checklist after this one.)	0	1	9

		Code Response					
2.	Code and describe professional treatment:	0	1	2	3	4	9

0. None

1. Inpatient: _____

2. Outpatient: _____

3. ECT: _____

4. Medication: _____

9. Unknown

3. Age of onset

4. Number of episodes — Episodes

5. Duration of longest episode in weeks — Weeks

Code Response

6. Rate and code impairment or incapacitation: 0 1 2 9

   0. None
   1. Impaired
   2. Incapacitated
   9. Unknown

7. Interviewer judgment on reliability of this information: 1 2 3

   1. Good
   2. Fair
   3. Poor

PSYCHOSIS

Code for a single episode (best recalled, worst episode if possible).

1. *What were his/her unusual beliefs or experiences?*

Specify: _____

_____77_____

—

	Did he/she ever…	No	Yes	Unk
1.a)	*…believe people were following him/her, or that someone was trying to hurt or poison him/her?*	0	1	9
1.b)	*…believe someone was reading his/her mind?*	0	1	9
1.c)	*…believe he/she was under the control of some outside person or power or force?*	0	1	9
1.d)	*…believe his/her thoughts were broadcast, or that an outside force took away his/her thoughts or put thoughts into his/her head?*	0	1	9
1.e)	*…have any other strange or unusual beliefs?*	0	1	9

If yes: Describe: _____

_____

1.f)	*…see things that were not really there?*	0	1	9
1.g)	*…hear voices or other sounds that were not real?*	[0]	1	9

If yes: Describe: _____

_____

Skip to question 1.h

		No	Yes	Unk
1.g.1)	(Code **YES** if: voice with content having no relation to depression or elation, or voice keeping up running commentary on subject's behavior or thoughts, or two or more voices conversing.)	0	1	9
1.h)	*…speak in a way that was difficult to make sense of?*	0	1	9

If yes: Describe: _____

_____

1.i)	*…seem to be physically stuck in one position, or move around excitedly without any purpose?*	0	1	9

1.j) *...appear to have no emotions, or inappropriate emotions?* 0 1 9

2. *How long did the longest of these experiences last?* Weeks

INTERVIEWER: If less than 1 week (unless successfully treated), STOP HERE. Otherwise continue, if informant is knowledgeable about this person.

INTERVIEWER: If subject did NOT have any episode of Major Depression or Mania (by FIGS checklists from this informant), skip to question 6.

	No	Yes	Unk
3. *When any* (SX above) *happened, did he/she also have the mood disturbance we discussed before, at the same time?*	0	1	9

Skip to question 6

INTERVIEWER: For the rest of this checklist, "illness duration" refers to total time of illness, including active and prodromal and/or residual symptoms and/or treatment (include time on medication).

	No	Yes	Unk
4. (Probe and code YES if mania and/or depression lasted at least 30% of total duration of illness described above, or medication for it.)	0	1	9
5. (Probe and code YES if illness described above, or medication for it, was ever present for as long as one week, without depression and/or mania.)	0	1	9

Skip to question 6

5.a) (Code YES if the above was true for as long as two weeks.) 0 1 9

Code Response

6. Code and describe professional treatment (Code and describe all that apply): 0 1 2 3 4 9

   0. None
   1. Inpatient: _____
   2. Outpatient: _____
   3. ECT: _____
   4. Medication: _____
   9. Unknown

   Describe details and/or other treatment:

Age

7. Age of onset

Episodes

8. Number of episodes (Code 001 if chronic symptoms and/or treatment since onset)

9. Total illness duration (all episodes, includes active and prodromal and/or residual symptoms and/or treatment.

Weeks OR Years

Code Response

10. Rate and code impairment or incapacitation: 0 1 2 9

    0. None
    1. Impaired
    2. Incapacitated
    9. Unknown

11. Interviewer judgement on reliability of this information: 1 2 3

    1. Good
    2. Fair
    3. Poor

INTERVIEWER: If informant apparently does not know subject well enough to give information on Prodromal/Residual symptoms, STOP HERE.

If duration criterion for DSM III-R Schizophrenia, Chronic Type, already met, (question 9, total illness duration > 2 years), STOP HERE.

INTERVIEWER: Use this page only if Schizo-affective is ruled out (by questions 3 to 5 above), or if the psychosis symptoms lasted at least one week (or shorter duration if successfully treated).

Establishing the Prodromal Period:

16. *Now I would like to ask you about the year before his/her* (**psychotic symptoms**) *started. During that time did he/she…*

(Ask after completing question 16.a-n for the Prodromal perio

Establishing the Residual Period:

Now I would like to ask you about the year after his/her (**psychotic symptoms**) *stopped. During that time did he/she..*

	Prodromal Period			Residual Period		
	No	Yes	Unk	No	Yes	Unk
16.a) …*stay away from family and friends, become socially isolated?*	0	1	9	0	1	9
16.b) …*have trouble doing his/her job, going to school, or doing work at home?*	0	1	9	0	1	9
16.c) …*do something peculiar like talking to self in public?*	0	1	9	0	1	9
16.d) …*neglect hygiene and grooming?*	0	1	9	0	1	9
16.e) …*appear to have no emotions or inappropriate emotions?*	0	1	9	0	1	9
16.f) …*speak in a way that was hard to understand, or was he/she at a loss for words?*	0	1	9	0	1	9
16.g) …*have unusual beliefs or ideas?*	0	1	9	0	1	9
16.h) …*have unusual perceptions, like sensing the presence of a person not actually present?*	0	1	9	0	1	9
16.i) …*have no interests, no energy?*	0	1	9	0	1	9
16.j) …*find special meaning in TV, radio, or newspaper articles?*	0	1	9	0	1	9
16.k) …*feel nervous with other people?*	0	1	9	0	1	9
16.l) …*worry that people were out to get him/her?*	0	1	9	0	1	9

17.a) *How long did he/she have these experiences?* — Weeks: [ ][ ][ ]

INTERVIEWER: Return to top of question 16 to establish the Residual period and code in Residual Column.

17.b) *How long did he/she have these experiences after his/her* (**Active psychotic features**) *stopped?* — Weeks: [ ][ ][ ]

No Yes Unk

18. *Was he/she always this way?* 0 1 9

Code based on Informant's Report:

Did person being described have:			No	Yes	Unk
1.	**Depression**		0	1	9
	1.a)	Single	0	1	9
	1.b)	Recurrent	0	1	9
	1.c)	Impaired/Incapacitated	0	1	9
	1.d)	Treatment	0	1	9
	1.e)	Age of onset		Age	
2.	**Mania**		0	1	9
	2.a)	Single	0	1	9
	2.b)	Recurrent	0	1	9
	2.c)	Impaired/Incapacitated	0	1	9
	2.d)	Treatment	0	1	9
	2.e)	Age of onset		Age	
3.	**Psychosis**		0	1	9
	3.a)	(1) Chronic or (2) acute?	1	2	
	3.b)	Outside of mood disorder	0	1	9
	3.c)	Treatment	0	1	9
	3.d)	Age of onset		Age	

Appendix M Patient consent form

FOLLOW-UP STUDY

UNDERSTANDING THE CAUSES AND OUTCOME OF MENTAL HEALTH PROBLEMS

Please read this carefully if you wish to participate in our study.
Your participation is entirely voluntary

Consent form and general information sheet for participants

About six years ago you made contact with psychiatric services for the first time in your life. We would like to come and speak to you to find out how you are now, and ask you about any difficulties or problems that you may be having, or may have had over the last six years. As part of the AESOP study, we are also trying to find out more about the changes in concentration, memory and thought that happen in mental illness and how those changes relate to the symptoms and long-term outcome of the illness. We would also like to do some concentration and memory tests, which take about two hours. We would also like to ask you some questions about your behaviour in childhood and adulthood, and whether you have experienced any aggressive behaviour in adulthood. These tests will be similar to the ones you did six years ago. Normally, all the interviews and assessments will be completed over three appointments, each lasting about 2 ½ hours.

Anything you say will be treated in the strictest confidence. You will not be identified by name, but by a code number. If you decide not to be part of the study, this will not affect in any way the care you receive. If you do decide to take part you are free to withdraw from the study at any time without having to say why. Withdrawal from the study will not affect in any way, the care you receive. We hope you will agree to take part in this study so that your help may contribute to improving the care offered by hospitals. Participation in the study may not be of direct benefit to you, but may prove beneficial to others. If you would like to ask any questions or want to find out about anything else at all, please telephone Ms Jolanta Zanelli on 020 7848 0534 (see further contact details below). If she is not there when you call, other members of the research team will be happy to speak to you.

Consent section

I agree to being interviewed for this study. I understand that my participation is entirely voluntary and that I can withdraw from the interviews at any stage and that it will not affect any treatment that I may be receiving.

Signed …….
Date …….

I confirm that the person above has been given all the information provided on this information sheet and that they have agreed to participate in the study.

Witness …….
Date ……

Contact: Ms Jolanta Zanelli (020 7848 0534)
Section of General Psychiatry PO63
Institute of Psychiatry
De Crespigny Park, London SE5 8AF

AESOP Research Team:

Principal Investigator:	Prof. Robin Murray
Dr Paola Dazzan	Dr Paul Fearon
Dr Julia Lappin	Dr Craig Morgan
Dr Kris Naudts	Ms Helen Fisher
Dr Rina Dutta	

Appendix N Life chart

AMENDED LIFE CHART SCHEDULE

CLINICAL COURSE AND SYMPTOMS

CURRENT MENTAL STATE □
Is the patient now (last 30 days) in a psychotic episode?
0 = No
1 = Yes
2 = Yes, but not continuous with episode in inclusion

REMISSION
a) What is longest period (in weeks) during which the patient has had a remission of psychotic symptoms? □
b) Has the patient had a remission of psychotic symptoms for a period of at least **6 months** since the initial evaluation? □
0 = No 1 = Yes
b) **If YES above**, for how many weeks was the patient in the episode of inclusion (i.e. baseline episode) □

USUAL SYMPTOM SEVERITY (during psychotic episodes only) □
0 = No further episodes
1 = Mild
2 = Moderate
3 = Severe
Note: Use SCAN rating criteria
'The severity of a symptom can be assessed in terms of duration, persistence, degree of interference with other mental functions, distress, impairment of everyday activities, effect on other people, and contact with services of various kinds.'
SCAN Rating Scales
0 Symptom(s) did not occur during period
1 Symptom(s) definitely occurred during period, but probably uncommon or transitory OR of such a minor degree it is not appropriate for use in classification
2 Symptom(s) definitely present, on multiple occasions or for part of time, during period AND at a level sufficient to use in classification
3 Symptom was more or less continuously present throughout the period/episode AND present in severe form

PRESENCE OF NEGATIVE SYMPTOMS □
0 = No
1 = Yes, for less than 6 months
2 = Yes, for more than 6 months
i.e. a) Marked reduction or loss of interests, initiative and drive, leading to serious deterioration of the performance of usual activities and tasks b) Emergence or marked exacerbation of social withdrawal (active avoidance of communication with other people) e) Gross and persistent self-neglect

COURSE TYPE □
1 = **Episodic**, no episode lasted over 6 months
2 = **Continuous**, no remission lasted over 6 months (Primarily symptoms A)
3 = **Continuous**, no remission lasted over 6 months (Primarily symptoms B)
4 = **Continuous**, no remission lasted over 6 months (Primarily symptoms A & B)
5 = **Neither episodic nor continuous**, at least 1 episode & 1 remission lasted over 6 months

NUMBER OF PSYCHOTIC EPISODES (Do NOT include first episode) □
(See Appendix 1 for definition of psychotic episode. Each "psychotic episode" must be separated by at least **6 months** spent in remission).
00 = Patient presently in remission from episode of inclusion

MONTHS OF LONGEST PSYCHOTIC EPISODE □

NON-PSYCHOTIC EPISODE(S) □
(Only rate if treatment was received)
0 = No
1 = Yes
If yes, include details (i.e. type of non-psychotic episode and number of episodes):

SUICIDE ATTEMPT(S) □
a) Rate the number of suicide attempts by the patient since the index episode of evaluation (if in any doubt re: intention, rate as deliberate self-harm)
0 = None

DELIBERATE SELF-HARM □
a) Rate the number of episodes of deliberate self-harm by the patient since the index episode of evaluation (if in any doubt re: intention, rate as deliberate self-harm)
0 = None
b) Record details of suicide attempts and episodes of deliberate self-harm

DRUG ABUSE/DEPENDENCE □
a) Rate illicit drug taking and/or abuse of illicit drugs over life course
0 = None
1 = Sporadic drug taking or occasional abuses reported, no evidence for frequent or regular use (i.e. less than one month)
2 = Sporadic drug taking or occasional abuses reported, but there is reason to suspect frequent or regular use (i.e. more than one month)
3 = Frequent or regular use definitely present (i.e. more than one month)
4 = Substance abuse (Maladaptive use leading to any of the following:
(1) failure to fulfil major role obligations due to substance
(2) substance exacerbating or leading to social or interpersonal problems
(3) recurrent abuse when physically hazardous (e.g. driving) or substance related legal problems)
5=Substance dependence (Maladaptive use leading to 3 of the following:
(1) increased tolerance
(2) symptoms of withdrawal
(3) substance taken in larger amounts over a longer period than originally intended
(4) persistent desire or unsuccessful attempts to cut down
(5) much time spent in activities to obtain the substance or recovering from effects
(6) impairment of social, occupational or recreational activities due to substance
(7) persistent use despite harmful physical or psychological effects of substance.
7 = Drug taking a definite possibility but impossible to assess the frequency and extent of use

b) If a rating of 1, 2, 3, 4,5 or 7 was made above, specify whatever information is available about the nature of the substance(s) taken by the patient. For each substance used, specify age of first use.
0 = No
1 = Yes
2 = Suspected/uncertain
8 = Not applicable/not inquired
9 = No information/impossible to assess

	Age 1st Used
Morphine or heroin	_____
Opium	_____
Amphetamines or derivatives	_____
Hashish or marijuana	_____
Hallucinogens (LSD and others)	_____
Cocaine and cocopaste	_____
Barbituates	_____
Non-barbiturate sedatives and tranquillisers	_____
Other, specify	_____

c) if a rating of 4 or 5 was made date periods of substance abuse or dependence
Period 1_____
Period 2_____
Period 3_____
Period 4_____

ALCOHOL ABUSE/DEPENDENCE □

a) Rate the patient's drinking habits over life course
0 = Does not drink at all
1 = Only occasional social drinking (mean 10 units or less per week)
2 = Moderate alcohol use (mean 21 units or less per week)
3 = Excessive alcohol use (mean more than 21 unit per week regularly)
4 = Alcohol abuse (Maladaptive use leading to any of the following:
(1) failure to fulfil major role obligations due to alcohol
(2) substance exacerbating or leading to social or interpersonal problems
(3) recurrent abuse when physically hazardous (e.g. driving) or alcohol related legal problems)
5 = Alcohol dependence (Maladaptive use leading to 3 of the following
(1) increased tolerance
(2) symptoms of withdrawal
(3) alcohol taken in larger amounts over a longer period than originally intended
(4) persistent desire or unsuccessful attempts to cut down
(5) much time spent drinking the substance or recovering from effects
(6) impairment of social, occupational or recreational activities due to alcohol
(7) persistent use despite harmful physical or psychological effects of alcohol
9 = No information/Not known

b) If a rating of 3, 4, 5 or 7 was made above, specify whatever information is available about the nature of the substance(s) taken by the patient

c) if a rating of 4 or 5 was made date periods of alcohol abuse or dependence
Period 1_____
Period 2_____
Period 3_____
Period 4_____

SERVICE USE AND TREATMENT

HAS THE PATIENT BEEN IN CONTACT WITH SERVICES AT ANY POINT DURING THE FOLLOW-UP PERIOD? □
0 = No
1 = Yes
If **YES**, continue

If **NO**, is this because: □
0 = None were offered
1 = Patient did not attend
If 1, specify reasons for this:
_____
_____
_____

TOTAL NUMBER OF HOSPITAL ADMISSIONS
@ f.u. □
@ 6 yrs □
@ 3 yrs □

TOTAL NUMBER OF PERIODS OF COMMUNITY TREATMENT
@ f.u. □
@ 6 yrs □
@ 3 yrs □

INPATIENT – complete one of these for each admission
3.2.1 Date of Admission □
3.2.2 Date of Discharge □
3.2.3 Ward Type □
3.2.4a MHA Status on Admission □
3.2.4b MHA Status during Admission □
3.2.5 MHA Section(s) □
3.2.6 Source of Referral □
3.2.7 Reason for Admission □
3.2.8 Family involvement □
3.2.9 Police or CJA Involvement □

OUTPATIENT – complete one of these for each outpatient period
3.3.1 Date of Referral □
3.3.2a Date Last Seen □
3.3.2b Date of Discharge or Hospital Admission □
3.3.3 Source of Referral □
3.3.4 Type of Contact □
3.3.5 Reason Contact Ended □

OTHER TREATMENT ITEMS
Overall Compliance/Attendance □
Rate patient's compliance/attendance at community/follow-up services
1 = Regular compliance/attendance [1-33% missed appointments]
2 = Irregular compliance/attendance [34-66% missed appointments]
3 = None compliance/attendance [67-100% missed appointments]

Reason for Irregular or None Attendance
What was the reason(s) why the patient did not fully attend follow-up appointments?

Current treatment status
Patient's treatment status at the time of interview
@ f.u. □
@ 6 yrs □
@ 3 yrs □

0 = Not in any form of treatment
1 = Inpatient psychiatric facility (includes general hospital psychiatric wards)
2 = Standard outpatient/CMHT
3 = Assertive outreach
4 = Acute home treatment/crisis intervention
5 = Other, specify
6 = More than one above, specify

Traditional treatment □

A great variety of traditional healing practices exists and the particular form applied should be described in a narrative
0 = No
1 = Yes
9 = Uncertain
Give details below:

SOCIODEMOGRAPHIC CHANGES DURING THE FOLLOW-UP PERIOD

TYPE OF LIVING ARRANGEMENTS
No. of changes following first episode interview
Type of living arrangements
No. of people in household
Approx. length of residence (in weeks)

MONTHS IN PRISON DURING FOLLOW-UP PERIOD □

ANY OTHER SUGGESTIONS OF ANTI-SOCIAL/OFFENDING BEHAVIOUR? □
0 = No 1 = Yes

TYPE OF ACCOMMODATION AT FOLLOW-UP □
0 = Self/joint owner occupied
1 = Family owner occupied
2 = Private rented
3 = Local Authority rented
4 = Housing Association rented
5 = Other (specify)

CURRENT MARITAL STATUS □
Rate the patient's current marital status
0 = Married or common law marriage
1 = In steady relationship
2 = Single, no partner
3 = Divorced
4 = Separated
5 = Widowed
6 = Other, specify

MAIN MARITAL STATUS DURING FOLLOW-UP PERIOD □
Rate the patient's main marital status during follow-up period
0 = Married or common law marriage
1 = In steady relationship
2 = Single, no partner
3 = Divorced
4 = Separated
5 = Widowed
6 = Other, specify

CURRENT PARENTAL STATUS
Rate patient's current parental status
0 = No children
1 = Parent, living with partner
2 = Single parent
3 = Parent, children live with other parent
4 = Parent, children live with relatives
5 = Parent, children in care

PAST PARENTAL STATUS □
Rate patient's parental status during majority of follow-up period
0 = No children
1 = Parent, living with partner
2 = Single parent
3 = Parent, children live with other parent
4 = Parent, children live with relatives
5 = Parent, children in care

CURRENT EMPLOYMENT STATUS (LAST 30 DAYS) □
Has the patient been employed at a paid job (i.e. an earning occupation) in the last 30 days?
0 = No
1 = Yes, specify job
2 = Student

REASONS FOR CURRENT UNEMPLOYMENT (LAST 30 DAYS) □
If the patient has not had a paid job in the last 30 days, rate the reasons for unemployment
0 = Related to the patient's mental illness (inc.'s hospitalisation, simple refusal to work, etc.)
1 = Unrelated to the patient's mental illness
2 = Other, specify
3 = Combination of the above, specify

PAST EMPLOYMENT □
Rate employment (or earning job) since index episode (exclude last 30 days)
0 = Has been employed 75-100% of the time
1 = Has been employed 50-75% of the time
2 = Has been employed 25-50% of the time
3 = Has been employed 0-25% of the time

REASONS FOR PAST UNEMPLOYMENT □
Rate reason for unemployment since index episode (exclude last 30 days)
0 = Related to the patient's mental illness (inc.'s hospitalisation, simple refusal to work, etc.)
1 = Unrelated to the patient's mental illness
2 = Other, specify
3 = Combination of the above, specify

EDUCATION □
Since the index episode has the patient undertaken an educational programme (including vocational training), of at least 10 weeks duration?
0 = No
1 = Yes

SOCIAL NETWORK: CHANGES

HAS THE PATIENT'S RELATIONSHIP WITH FAMILY/FRIENDS BEEN AFFECTED BY HIS/HER ILLNESS? □
(NB: Friends here refers only to very close friends the patient had at baseline)
1 = Yes
2 = No

IF YES, HOW □
1 = Increased frequency of contact
2 = Decreased frequency of contact

FOR EITHER OF THE ABOVE, DETERMINE THE DEGREE OF CHANGE □
1 = To a large extent (e.g. change from low to high frequency or vice versa)
2 = To a moderate extent (e.g. change from medium to high frequency or vice versa)
3 = To a small extent (e.g. change from low to medium frequency or vice versa)
ENSURE THAT THE CHANGE IS FROM THE PRE-MORBID follow-upNCTIONING LEVEL.

IF THE PATIENT SEES LESS OF ANY FAMILY MEMBER(S)/FRIEND(S), WHY IS THIS?
0 = Because of illness □
1 = Family quarrels
2 = Moved away
3 = Drifted apart
4 = Died
5 = Other, specify

SOCIAL NETWORK: CURRENT

HOW OFTEN DO YOU VISIT OR SPEAK TO FAMILY/FRIEND(S)? □

0 = Daily 3 = Monthly
1 = Weekly 4 = < than above
2 = Fortnightly 5 = Never

DO YOU HAVE ANY CLOSE CONFIDANTS? □

1 = Yes 2 = No

HOW OFTEN DO YOU VISIT/SPEAK TO CONFIDANTS? □

0 = Daily 4 = < than above
1 = Weekly 5 = Never
2 = Fortnightly
3 = Monthly

FATHER'S EMPLOYMENT AT BIRTH

What was the main job of the subject's father when the subject was born?

_____

_____

PATIENTS WHO DIED SINCE THE INITIAL EVALUATION

Date of death

Was the death medically certified? □
0 = No
1 = Yes
9 = No information/not known

Cause of death_____

Immediate cause (if known) _____

Underlying cause (if known) _____

Contributory cause(s) (if known) _____

If death was due to suicide, specify method □
0 = Death not due to suicide
1 = Self-poisoning with medicaments
2 = Firearms
3 = Hanging
4 = Jumping from heights
5 = Stabbing
6 = Drowning
7 = Other, specify
9 = Not known

Antipsychotic Treatment over follow-up period

Complete one for each medication
1. Name of antipsychotic:
Dose and delivery method
Date of commencement:
Date of treatment discontinuation:
Time on treatment (weeks):
Reason for discontinuation:
[1= change to alternative antipsychotic; 2= discontinued by treating physician;
3=discontinued by patient; 4=other]
Adherence to antipsychotic over this period:
[1 (0-33%) ; 2 (33-67%) ; 3 (67-100%)]

Appendix O Risk factors adjusted analyses

Table: Adjusted odds ratios adjusted for gender, age, centre and ethnicity and 95% CIs for baseline diagnosis of PMD, schizophrenia and bipolar compared with controls

	PMD (n72) vs. controls			Schizophrenia (n218) vs. controls			Bipolar (n70) vs. controls		
	Adjusted OR (2dp)	**95% CI (2dp)**	**P (3dp)**	**Adjusted OR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**Adjusted OR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Place of birth:									
UK	1.0	-	-	1.0	-	-	1.0	-	-
Non-UK	1.20	0.53-2.72	0.667	0.93	0.55-1.57	0.787	0.55	0.23-1.31	0.176
Relationship Status:									
Stable relationship	1.0	-	-	1.0	-	-	1.0	-	-
Single	2.05	1.19-3.53	0.009	5.05	3.29-7.75	<0.001	2.07	1.16-3.69	0.014
Ever had a long term relationship:									
Yes	1.0	-	-	1.0	-	-	1.0	-	-
No	1.67	0.79-3.50	0.178	3.37	2.10-5.41	<0.001	2.54	1.27-5.08	0.008
Living with:									
With people	1.0	-	-	1.0	-	-	1.0	-	-
Alone	1.41	0.81-2.47	0.222	2.44	1.64-3.63	<0.001	2.34	1.35-4.06	0.003
Level of Education:									
Higher	1.0	-	-	1.0	-	-	1.0	-	-
Further	0.98	0.39-2.48	0.967	1.66	0.93-2.99	0.088	1.16	0.55-2.43	0.692
School	2.42	1.07-5.43	0.033	3.01	1.44-5.12	<0.001	0.95	0.46-1.99	0.894
Employment Status:									
Employed and other	1.0	-	-	1.0	-	-	1.0	-	-
Unemployed	1.68	0.98-2.86	0.057	3.44	2.30-5.15	<0.001	2.24	1.31-3.85	0.003
Ever worked									
Yes	1.0	-	-	1.0	-	-	1.0	-	-
No	0.79	0.13-4.94	0.799	1.88	0.59-5.96	0.283	1.08	0.28-4.21	0.915
Contact with friends:									

	PMD (n72) vs. controls			Schizophrenia (n218) vs. controls			Bipolar (n70) vs. controls		
	Adjusted OR (2dp)	**95% CI (2dp)**	**P (3dp)**	**Adjusted OR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**Adjusted OR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Daily – monthly	1.0	-	-	1.0	-	-	1.0	-	-
Never / less than monthly	4.17	1.71-10.17	0.002	10.89	5.88-20.18	<0.001	2.99	1.18-7.59	0.021
Contact with family:									
Daily – monthly	1.0	-	-	1.0	-	-	1.0	-	-
Never / less than monthly	3.15	0.88-11.25	0.077	2.77	0.97-7.94	0.058	1.70	0.33-8.84	0.526
Close confidants:									
Yes	1.0	-	-	1.0	-	-	1.0	-	-
No	4.45	2.11-9.41	<0.001	10.93	6.24-19.16	<0.001	4.85	2.30-10.20	<0.001
Family history of any mental illness:									
No	1.0	-	-	1.0	-	-	1.0	-	-
Yes	5.49	2.70-11.16	<0.001	7.77	4.53-13.32	<0.001	10.90	5.44-21.85	<0.001
Family history of psychosis:									
No	1.0	-	-	1.0	-	-	1.0	-	-
Yes	5.83	2.36-14.38	<0.001	11.00	5.76-21.00	<0.001	7.87	3.41-18.13	<0.001
Parental history of any mental illness:									
No	1.0	-	-	1.0	-	-	1.0	-	-
Yes	6.71	2.53-17.82	<0.001	9.62	4.60-20.11	<0.001	10.40	4.19-25.80	<0.001
Parental history of psychosis:									
No	1.0	-	-	1.0	-	-	1.0	-	-
Yes	7.17	2.13-24.19	0.001	12.45	4.95-31.28	<0.001	7.91	2.51-24.98	<0.001
Life Events									
No	1.00	-	-	1.0	-	-	1.0	-	-
Yes	5.25	1.64-16.82	0.005	2.17	0.77-6.14	0.144	3.94	1.19-13.03	0.025
Life Difficulties:									
No	1.00	-	-	1.0	-	-	1.0	-	-
Yes	3.42	1.00-11.77	0.051	3.42	1.40-8.15	0.005	0.97	0.25-3.71	0.960
Childhood Adversity:									
No	1.0	-	-	1.0	-	-	1.0	-	-
Yes	1.30	0.58-2.94	0.522	6.42	2.71-15.23	<0.001	1.36	0.60-3.11	0.459
Number of Childhood Adversity Factors	1.07	0.81-1.40	0.642	1.27	1.08-1.49	0.004	1.12	0.87-1.43	0.390

Table: Adjusted odds ratios adjusted for gender, age, centre and ethnicity and 95% CIs for lifetime diagnosis of PMD, schizophrenia and bipolar compared with controls

	PMD (n51) vs. controls			Schizophrenia (n225) vs. controls			Bipolar (n73) vs. controls		
	aOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**aOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**aOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Place of birth:									
UK	1.00	-	-	1.00	-	-	1.00	-	-
Non-UK	1.00	0.40-2.51	0.995	0.96	0.56-1.65	0.886	0.55	0.22-1.36	0.197
Relationship Status:									
Stable relationship	1.00	-	-	1.00	-	-	-	-	-
Single	1.69	0.91-3.13	0.096	5.36	3.46-8.28	<0.001	2.03	1.16-2.57	0.014
Ever had a long term relationship:									
Yes	1.00	-	-	1.00	-	-	1.00	-	-
No	1.67	0.69-4.04	0.255	4.08	2.51-6.63	<0.001	2.08	1.04-4.16	0.038
Living with:									
With people	1.00	-	-	1.00	-	-	1.00	-	-
Alone	2.26	1.21-4.23	0.011	2.93	1.97-4.37	<0.001	1.27	0.71-2.28	0.426
Level of Education:									
Higher	1.00	-	-	1.00	-	-	1.00	-	-
Further	1.68	0.57-4.93	0.347	1.65	0.90-3.04	0.107	1.18	0.57-2.45	0.658
School	2.89	1.08-7.74	0.035	3.34	1.91-5.84	<0.001	0.98	0.48-1.98	0.946
Employment Status:									
Employed and other	1.00	-	-	1.00	-	-	1.00	-	-
Unemployed	2.12	1.13-3.96	0.019	4.33	2.87-6.53	<0.001	1.58	0.94-2.64	0.082
Ever worked									
Yes	1.00	-	-	-	-	-	1.00	-	-
No	<0.01	<0.01-<0.01	<0.001	2.45	0.77-7.76	0.129	0.95	0.24-3.72	0.937
Contact with friends:									
Daily – monthly	1.00	-	-	1.00	-	-	1.00	-	-
Never / less than monthly	4.24	1.62-11.14	0.003	12.59	6.66-23.78	<0.001	1.77	0.57-5.44	0.321
Contact with family:									
Daily – monthly	1.00	-	-	1.00	-	-	1.00	-	-
Never / less than monthly	1.83	0.34-9.94	0.482	5.58	2.13-14.60	<0.001	1.05	0.13-8.50	0.965

	PMD (n51) vs. controls			Schizophrenia (n225) vs. controls			Bipolar (n73) vs. controls		
	aOR (2dp)	**95% CI (2dp)**	**P (3dp)**	**aOR (2dp)**	**95% CI (2dp)**	**P (3dp)**	**aOR (2dp)**	**95% CI (2dp)**	**P (3dp)**
Close confidants:									
Yes	1.00	-	-	1.00	-	-	1.00	-	-
No	4.71	2.08-10.68	<0.001	11.32	6.37-20.10	<0.001	2.72	1.14-6.48	0.024
Family history of any mental illness:									
No	1.00	-	-	1.00	-	-	1.00	-	-
Yes	10.68	5.06-22.52	<0.001	6.96	4.10-11.84	<0.001	13.19	6.64-26.20	<0.001
Family history of psychosis:									
No	1.00	-	-	1.00	-	-	1.00	-	-
Yes	12.85	5.24-31.51	<0.001	10.16	5.37-19.25	<0.001	8.67	3.87-19.44	<0.001
Parental history of any mental illness:									
No	1.00	-	-	1.00	-	-	1.00	-	-
Yes	11.67	4.29-31.75	<0.001	7.59	3.72-15.47	<0.001	14.71	6.15-35.17	<0.001
Parental history of psychosis:									
No	1.00	-	-	1.00	-	-	1.00	-	-
Yes	12.73	3.85-42.08	<0.001	9.63	3.96-23.41	<0.001	11.52	3.96-33.52	<0.001
Life Events									
No	1.00	-	-	1.00	-	-	1.00	-	-
Yes	3.32	0.96-11.45	0.058	2.86	0.97-8.44	0.056	5.56	1.97-15.71	0.001
Life Difficulties:									
No	1.00	STATA unable to calculate due to numbers being so low		1.00	STATA unable to calculate due to numbers being so low		1.00	STATA unable to calculate due to numbers being so low	
Yes	2.71			3.36			3.61		
Childhood Adversity:									
No	1.00	-	-	1.00	-	-	1.00	-	-
Yes	2.57	1.02-6.44	0.045	2.97	1.41-6.25	0.004	1.55	0.65-3.71	0.323
Number of Childhood Adversity Factors	1.26	1.02-1.57	0.036	1.21	1.03-1.42	0.020	1.15	0.91-1.46	0.241

Appendix P Outcome results

Death - n320/368

Table 8-3: Comparison of deaths by lifetime diagnosis

	PMD (n44)	SAD (n17)	SZ (n196)	BP (n63)
	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Dead	4/44 (9.1)	1/17 (5.9)	12/196 (6.1)	5/63 (7.9)

SZ=schizophrenia; BP=bipolar

Table 8-4: OR, CI and p value for comparisons between the groups in the proportion of cases who died over follow-up

	PMD vs. SZ (n240)	PMD vs. BP (n107)	PMD vs. SAD (n61)	SAD vs. SZ (n213)	SAD vs. BP (n80)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Death	1.53 (0.47-5.00)	1.16 (0.29-4.59)	1.60 (0.17-15.44)	0.96 (0.12-7.85)	0.73 (0.08-6.66)

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval; $ Unable to calculate odds ratios as no SAD cases died over follow-up.

Completed suicide – n15/22

Table 8-5: Comparison of completed suicide outcome variables by lifetime diagnosis

	PMD (n3)	SAD (n1)	SZ (n7)	BP (n4)
	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Completed suicides	1/3 (33.3)	1/1 (100)	5/7 (71.4)	2/4 (50.0)

SZ=schizophrenia; BP=bipolar

Table 8-6: OR, CI and p value for comparisons between the groups in the completed suicide proportions over follow-up

	PMD vs. SZ (n10)	PMD vs. BP (n7)	PMD vs. sad (n4)	SAD vs. SZ (n8)	SAD vs. BP (n5)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Death	5.0 (0.27-91.52)	2.0 (0.09-44.35)	$	$	$

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval; $ Unable to calculate odds ratios as all the SAD cases committed suicide.

Employment status – n257/368

Table 8-7: Comparison of employment status by lifetime diagnosis

	PMD (n30)	SAD (n15)	SZ (n165)	BP (n47)
	n (%)	n (%)	n (%)	n (%)
Employment status during fu:				
Employed 75-100%	8 (26.7)	2 (13.3)	15 (9.1)	11 (23.4)
Employed 50-75%	4 (13.3)	1 (6.7)	6 (3.6)	13 (27.7)
Employed 25-50%	3 (10.0)	0 (0)	16 (9.7)	2 (4.3)
Employed 0-25%	15 (50.0)	12 (80.0)	128 (77.6)	21 (44.7)

SZ=schizophrenia; BP=bipolar

Table 8-8: OR, CI and p value for comparisons between the groups of the employment status over the follow-up period

	PMD vs. SZ (n195)	PMD vs. BP (n77)	PMD vs. SAD (n45)	SAD vs. SZ (n180)	SAD vs. BP (n62)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Employed 0-25%	0.29 (0.13-0.65)***	1.24 (0.49-3.10)	0.25 (0.06-1.07)*	1.16 (0.31-4.32)	4.95 (1.23-19.88)**
Employed 75-100%	3.64 (1.38-9.57)***	1.19 (0.41-3.41)	2.36 (0.43-12.87)	1.54 (0.32-7.47)	0.50 (0.10-2.58)

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

Total number of hospitalisations – n92/368

Table 8-9: Comparison of total hospitalisations by lifetime diagnosis

	PMD (n39)	SAD (n16)	SZ (n179)	Mania (n58)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Number of hospitalisations	1 (1-2)	2 (1-4)	3 (1-6)	2.5 (1-4)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 8-10: IRR, CI and p value for comparisons between the groups of the total hospitalisations over the follow-up period

	PMD vs. SZ (n218)	PMD vs. BP (n97)	PMD vs. SAD (n55)	SAD vs. SZ (n195)	SAD vs. BP (n74)
	IRR (CI)	IRR (CI)	IRR (CI)	IRR (CI)	IRR (CI)
Total number of hospitalisations	0.45 (0.31-0.65)***	0.53 (0.36-0.78)***	0.62 (0.33-1.17)	0.73 (0.45-1.18)	0.88 (0.55-1.40)

*p<0.1; **p<0.05; ***p<0.01; IRR = incidence rate ratio; CI = 95% confidence interval.

Percentage of follow-up spent as an inpatient – n250/368

Table 8-11: Comparison of percentage of the follow-up as inpatient data by lifetime diagnosis

	PMD (n36)	SAD (n12)	SZ (n149)	Mania (n53)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Percentage of follow-up as an inpatient	0.68% (0.07-3.28%)	2.06% (0.28-8.96%)	3.54% (1.29-11.13%)	1.80% (1.07-4.11%)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 8-12: Coefficient, CI and p value for comparisons between the groups of the percentage as an inpatient over the follow-up period

	PMD vs. SZ (n185)	PMD vs. BP (n89)	PMD vs. SAD (n48)	SAD vs. SZ (n161)	SAD vs. BP (n65)
	Coefficient (CI)	Coefficient (CI)	Coefficient (CI)	Coefficient (CI)	Coefficient (CI)
Percentage of follow-up as an inpatient	-4.71 (-8.74 to -0.69)**	0.02 (-3.82 to 3.86)	-4.80 (-14.39 to 4.78)	0.09 (-9.21 to 9.39)	4.82 (-3.80 to 13.44)

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

Ever having been admitted compulsorily – n246/368

Table 8-13: Comparison of compulsory hospitalisation data by lifetime diagnosis

	PMD (n34)	SAD (n12)	SZ (n147)	Mania (n53)
	N (%)	N (%)	N (%)	N (%)
Ever admitted compulsorily:				
No	17 (50.0)	6 (50.0)	41(27.9)	13 (24.5)
Yes	17 (50.0)	6 (50.0)	106 (72.1)	40 (75.5)

SZ=schizophrenia; BP=bipolar

Table 8-14: OR, CI and p value for comparisons between the groups of compulsory admissions

	PMD vs. SZ (n181)	PMD vs. BP (n87)	PMD vs. SAD (n46)	SAD vs. SZ (n159)	SAD vs. BP (n65)
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Compulsory admissions	0.39 (0.18-0.83)**	0.33 (0.13-0.81)**	1.00 (0.27-3.73)	0.39 (0.12-1.27)	0.33 (0.09-1.18)*

*p<0.1; **p<0.05; ***p<0.01; OR = odds ratio; CI = 95% confidence interval.

Total number of days hospitalised – n250/368

Table 8-15: Comparison of hospitalisation days data by lifetime diagnosis

	PMD (n36)	SAD (n12)	SZ (n149)	Mania (n53)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Total number of days hospitalised	25.2 (0-123)	74.5 (11-336.5)	130 (48-363)	69 (32-154)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 8-16: Coefficients, CI and p value for comparisons between the groups of the hospitalisation days over the follow-up period

	PMD vs. SZ (n185)	PMD vs. BP (n89)	PMD vs. SAD (n48)	SAD vs. SZ (n161)	SAD vs. BP (n65)
	Coefficient (CI)	Coefficient (CI)	Coefficient (CI)	Coefficient (CI)	Coefficient (CI)
Total number of days hospitalised	-224.76 (-316.06 to -133.46)***	-41.67 (-1.02.65 to 19.30)	-225.78 (-515.06 to 63.50)	1.02 (-301.39 to 303.42)	184.11 (-114.98 to 483.19)

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.

Percentage of hospitalisations involving the police – n219/368

Table 8-17: Comparison of police involvement in hospitalisation data by lifetime diagnosis

	PMD (n33)	SAD (n11)	SZ (n128)	Mania (n47)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Percentage of hospitalisations involving police	0 (0-0)	0 (0-50)	20 (0-55)	0 (0-54.5)

SZ=schizophrenia; BP=bipolar; IQR = Interquartile range.

Table 8-18: Coefficients, CI and p value for comparisons between the groups of police involvement in hospitalisations over the follow-up period

	PMD vs. SZ (n161)	PMD vs. BP (n80)	PMD vs. SAD (n44)	SAD vs. SZ (n139)	SAD vs. BP (n58)
	Coefficient (CI)	**Coefficient (CI)**	**Coefficient (CI)**	**Coefficient (CI)**	**Coefficient (CI)**
Percentage of hospitalisations involving police	-24.34 (-36.58 to -12.10)***	-18.28 (-33.54 to -3.01)**	-13.72 (-35.41 to 7.97)	-10.62 (-31.28 to 10.05)	-4.56 (-26.99 to 17.88)

*p<0.1; **p<0.05; ***p<0.01; CI = 95% confidence interval.